SUPPLEMENTARY MATERIALS

Supplementary Methods

Search strategy
Our PubMed search for each approved immunotherapy drug used the following search terms: (quality of life [MeSH Terms] OR quality of life [Text Word] OR patient reported outcomes [Text Word] AND drug approved name [All Fields]). If the trial protocol was not available online, we contacted the authors by email to ask for a copy. If no answer was received after follow-up, data were collected only from the published manuscripts. If discrepancies were found between the documents, information was taken first from the clinical study report, and then from the trial protocol.

Data collection
The data extraction sheet included 47 predefined evaluation criteria, which were divided into six categories: (a) general trial description, (b) reporting of research hypothesis and objectives, (c) PRO instruments, (d) clinical relevance, (e) statistical analysis, and (f) handling of missing data.

(a) General trial description

We reported the general characteristics of each trial, including whether it was randomized or single-arm, the line-of-therapy indication in the drug authorization, the sample size of the analyzed population. For the published manuscripts, we reported the impact factor (IF) of the journal of publication during the year of publication. Only the IF of the journal that published the manuscript reporting the main clinical trial result (the primary manuscript) was used for analyses if no separate PRO manuscript was published.

(b) Reporting of specific hypothesis and research objectives

For each trial that led to a drug receiving FDA approval, we reported whether a specific hypothesis that stated a direction, domain of interest, and specified time frame was defined to inform the analysis of the PRO endpoint. The definition of "broad hypothesis" was adopted from a previous systematic review.[14] We also reported whether the evaluation of PROs was stated as a primary, secondary, or exploratory endpoint in the trial's final protocol.

(c) PRO instruments

We identified the PRO instruments used in each clinical trial. We also reported the PRO collection method and whether the instruments were cancer site specific and validated.

(d) Clinical relevance

The threshold for clinical relevance was defined as a clinically meaningful within-patient or within-treatment-group change in PRO score from baseline over the course of therapy, or as a clinically meaningful difference in PRO scores between groups. We reported whether each study specified a threshold for clinical relevance and whether a reference that justified the threshold was cited.

(e) Statistical analysis

We reported the primary statistical techniques used to measure the outcomes of interest in each trial. We also reported whether a correction for type I error was done when needed and we determined whether a trial reported a completion/compliance rate of the PRO instruments.

(f) Handling missing data

We reported whether a method to handle missing data was defined in the trial protocol or in the methods section of the manuscript. We also reported whether a trial provided details about the reasons for missing data.

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Supplementary Table 1. Coding template: overview of all quality-assessment criteria

LABEL	EXPLANATION	CODES
General trial description		
ID	Original identification number of the clinical trial	Open ended (Number)
NCT number	NCT number of the clinical trial leading to FDA approval	Open ended (Nominal)
Drug name	Pharmaceutical and commercial drug name	Open ended (Nominal)
Approval date	Year of the FDA approval	Open ended (Year)
Approval type	The type of approval received for the drug was: Regular: Drug received regular FDA approval Accelerated: Drug received accelerated FDA approval	- Regular - Accelerated
Approval indication – Line of therapy	Line of therapy in specific diagnosis First line: The drug was approved as first line treatment Second line: The drug was approved as second line treatment End of line: The drug was approved as end of line treatment Adjuvant: The drug was approved as adjuvant treatment Maintenance: The drug was approved as maintenance treatment	- First line - Second line - End of line - Adjuvant - Maintenance
Approval indication – Alone or combination	FDA approval for the I-O drug alone or in combination: Alone: I-O drug was approved alone Combination: I-O drug was approved in combination with another agent	- Alone - Combination
First author	Last name of the first author of the clinical trial publication	Open ended
Year	Year of publication	Open ended (Year)
Journal name	Name of the journal that published the primary manuscript	Open ended (Nominal)
Journal impact factor	Impact factor of the journal that published the primary manuscript	Open ended (Number)
Manuscript type	Type of manuscript based on the outcomes that the article focuses on (clinical outcomes, PRO outcomes or both) Clinical trial: Article that reports clinical outcomes without PRO results PRO: Article that focuses on the PRO results, usually a secondary publication of the clinical trial Both: Article that reports both clinical outcomes and PRO results	- Clinical trial - PRO - Both
Full clinical trial protocol	Full clinical trial protocol available either in NCT or on the journal's website Yes: The full clinical trial protocol was available No: The full clinical trial protocol was not available	- Yes - No

Phase	Phase of the clinical trial Phase I: The clinical trial was a phase I trial Phase II: The clinical trial was a phase II trial Phase I/II: The clinical trial was a phase I/II trial Phase III: The clinical trial was a phase III trial	- Phase I - Phase II - Phase I/II - Phase III
Randomization status	Type of clinical trial Non-randomized: The clinical trial was not randomized Randomized: The clinical trial was randomized	- Non-randomized - Randomized
Type of tumor	The type of tumor investigated in the clinical trial	Open ended (Nominal)
Treatment arms	The number of treatment arms included in the clinical trial Single arm: The clinical trial was a single-arm study Multiple arm: The clinical trial was a multiple-arm study	- Single arm - Multiple arm
Sample size	Number of enrolled patients	Open ended (Number)
Publication date	Publication date of the primary manuscript	Open ended (MM/DD/YYYY)
Pubmed search results PRO	Number of PubMed results received using the keywords for PRO search: “quality of life[MeSH Terms] OR quality of life[Text Word] OR patient reported outcomes[Text Word] AND specific drug name[Text Word]"	Open ended (Number)
PRO first author	Last name of the first author of the PRO publication	Open ended (Nominal)
PRO pub date	Date of publication of the PRO results	Open ended (MM/DD/YYYY)
Journal name	Name of the journal that published the PRO manuscript	Open ended (Nominal)
Journal impact factor	Impact factor of the journal that published the PRO manuscript	Open ended (Number)
Limitations	The authors stated the limitations of the study Yes: The authors stated the limitations of the study No: The authors did not state the limitations of the study Not available: No PRO results published	- Yes - No - Not Available (no PRO)
PRO conclusion	PRO conclusion (compared to control arm or standard of care) Superior: Experimental arm is superior to control arm or standard of care Similar outcomes: Similar outcomes to control arm or standard of care Inferior: Experimental arm is inferior to control arm or standard of care Not reported: No conclusion in the manucript reported Not available: No PRO results published	- Superior - Similar outcomes - Inferior - Not reported - Not available (no PRO)

Reporting of specific hypothesis and research objectives		
PRO hypothesis	The extent to which the PRO research question is specified in the introduction of the article or the protocol of the clinical trial: None: No PRO hypotheses stated Specific: The direction of the PRO hypothesis is stated with the domain of interest and the time frame/amount of change Broad: The PRO hypothesis is stated broadly (no direction of the hypothesis, domains of interest, time frame, and/or amount of change) Not available: No PRO results published	- None - Specific - Broad - Not Available (no PRO)
PRO endpoint	The type of endpoint of the PRO outcome: Primary: The PRO outcome is reported as primary endpoint of the article Secondary: The PRO outcome is reported as secondary endpoint in the article Exploratory: The PRO outcome is reported as an exploratory endpoint in the article Uncertain: It is not clear from the article what type of endpoint the PRO outcome is Not available: No PRO results published	- Primary - Secondary - Exploratory - Uncertain - Not Available (no PRO)
PRO instruments		
PRO instrument	List all the instruments that were used to measure the PRO outcome	- Open ended (Nominal) - Not Available (no PRO)
PRO instrument validity	The PRO instruments used were referenced and cited in the manuscript Yes: The PRO instruments used were referenced and cited in the manuscript No: The PRO instruments used were not referenced and cited in the manuscript Not available: No PRO results published	- Yes - No - Not Available (no PRO)
Planned schedule of questionnaires administration	The planned schedule of questionnaire administration of the PRO instruments	- Open ended (Nominal) - Not Available (no PRO)

Baseline PRO	Did the article include a baseline assessment? Yes: There was report of a baseline PRO assessment No: There was no baseline PRO assessment Not reported/unclear: There was no clear report of baseline PRO assessment Not available: No PRO results published	- Yes - No - Not reported/unclear - Not Available (no PRO)
PRO collection method	Method of collecting PRO data from participant Paper: PRO data were collected using paper questionnaires Electronic: PRO data were collected using electronic devices Combination: PRO data were collected using both paper questionnaires and electronic devices Not reported: PRO data collection method was not reported Not available: No PRO results published	- Paper - Electronic - Combination - Not reported - Not Available (no PRO)
PRO site specific	The PRO instruments used were cancer site specific Yes: PRO instruments used were cancer site specific No: PRO instruments used were not cancer site specific Not available: No PRO results published	- Yes - No - Not Available (no PRO)
PRO dimensions	Targeted PRO dimensions: Single scale/dimension: PRO instruments were unidimensional Multiple scales/dimension: PRO instruments were multidimensional Not available: No PRO results published	- Single scale/dimension - Multiple scales/dimenstions - Not Available (no PRO)
Follow-up measures	Were two or more follow-up measures included in the primary PRO analysis? Yes: Two or more follow-up assessments included in primary PRO analysis No: Only one follow-up assessment included in primary PRO analysis Not reported: Number of follow-up assessments included in primary PRO analysis not reported/unclear from the article Not available: No PRO results published	- Yes - No - Not reported/unclear - Not Available (no PRO)

Clinical relevance		
Clinical relevance	The reported threshold for minimal clinically important difference, expressed either as a: Difference of X points: Clinical relevance was evaluated as a between-arms difference Change of X points: Clinical relevance was evaluated as a change within-person or within-arm	- Change of X points from baseline - Difference of X points between 2 arms - Not reported - Not Available (no PRO)
Clinical relevance justified	Was the clinical relevance defined and cited in the manuscript? Yes: The clinical relevance was defined and a reference was cited No: The clinical relevance was not defined and no reference was cited Not available: No PRO results published	- Yes - No - Not Available (no PRO)
Statistical analysis		
Primary statistical method	Main statistical method that was used for the primary analysis of the PRO endpoint	- Open ended (Nominal) - Not Available (no PRO)

Type I error	Was a procedure to control for type I error needed in the primary PRO analysis? Not needed: Control for type I error not necessary because primary PRO analysis was on a single time point and single dimension or used longitudinal analysis for a single dimension. Needed and done: Control for type I error was needed AND done Needed but not done: Control for type I error was needed, but not done. Not available: No PRO results published	- Not needed - Needed and done - Needed but not done - Not Available (no PRO)
Groups baseline PRO	Were treatment groups compared for PRO scores at baseline? Yes: A comparison of PRO scores at baseline between the treatment arms was made in the article No: There was no comparison of PRO scores at baseline between the treatment arms NA: Not applicable because clinical trial was single arm Not available: No PRO results published	- Yes - No - N/A - Not Available (no PRO)
Completion/Compliance rate	Were treatment arms compared for completion/compliance rates during the follow-up assessments? Yes: Compliance rates for the PRO follow-up assessments were reported per arm No: Compliance rates for the PRO follow-up assessments were not reported per arm Not available: No PRO results published	- Yes - No - Not Available (no PRO)
Completion/Compliance rate table	Did the authors provide a table summarizing completion/compliance rates for all arms and all time points? Yes: A compliance rates table was provided No: A compliance rates table was not provided Not available: No PRO results published	- Yes - No - Not Available (no PRO)

Dataset PRO analysis	The dataset that is used for the PRO main analysis was defined as: ITT: The intent-to-treat population mITT: A modified intent-to-treat population (mITT) Other 1: Patients with a baseline assessment and at least one post-baseline assessment Other 2: Patients who received at least one dose of study medication and completed at least one assessment. Other 3: ITT population with non-missing baseline measurements Unclear: Confusion arises from the article on what analysis population was used for primary analysis. Not reported: The analysis population for primary analysis was not reported and could not be deduced from the methodology/result section Not available: No PRO results published	- ITT - mITT - Other 1 - Other 2 - Other 3 - Unclear - Not reported - Not Available (no PRO)
Race ethnicity PRO	Manuscript reported on significant difference in PROs based on race and ethnicity of participants Yes: Manuscript reported on significant difference in PROs based on race and ethnicity of participants No: Manuscript did not report on significant difference in PROs based on race and ethnicity of participants Not available: No PRO results published	- Yes - No - Not Available (no PRO)
Handling missing data		
Missing data PRO	Manuscript reported approach for dealing with missing PRO assessments. Yes: Manuscript reported approach for dealing with missing PRO assessments No: Manuscript did not report approach for dealing with missing PRO assessments Not available: No PRO results published	- Yes - No - Not Available (no PRO)
Reasons missing PRO	The authors provided details on the reasons that led to missing PRO data by timepoint Yes: The authors provided details on the reasons that led to missing PRO data	- Yes - No - Not Available (no PRO)

	No: The authors provided details on the reasons that led to missing PRO data Not available: No PRO results published	

Abbreviations: FDA, Food and Drug Administration; I-O, immune-oncology; PRO, patient-reported outcomes.

Supplementary Table 2. Characteristics of individual clinical trials leading to drug approvals and of their corresponding PRO publications.

Information on clinical trials														
ID	NCT Number	First author	Pharmaceutical drug name	Cancer Type	Approval date (mm/dd/yy)	Approval type	Year of publication of the primary manuscript	Journal publishing the primary manuscript	Journal impact factor at time of publication	Clinical trial publication date (mm/dd/yy)	Published PRO data	Publication type	Total number of patients	Pubmed search results PRO
1	NCT02267603	Nghiem P[1]	Pembrolizumab	Merkel cell carcinoma	12/19/18	Accelerated	2019	Journal of Clinical Oncology	28.35	2/6/19	No	Clinical outcomes only	50	71
2	NCT02366143	Socinski MA[2]	Atezolizumab	NSCLC	12/6/18	Regular	2018	The New England Journal of Medicine	70.67	6/4/18	No	Clinical outcomes only	1202	18
3	NCT02702414	Zhu A[3]	Pembrolizumab	Hepatocellular carcinoma	11/9/18	Accelerated	2018	The Lancet Oncology	35.38	6/3/18	No	Clinical outcomes only	104	71
4	NCT02775435	Paz-Ares L[4]	Pembrolizumab + Carboplatin + Paclitaxel/nab-paclitaxel	NSCLC	10/30/18	Regular	2018	The New England Journal of	70.67	9/25/18	No	Clinical outcomes only	559	71

								Medicine						
5	R2810-ONC-1540	Migden M[5]	Cemiplimab-rwlc	Cutaneous squamous cell carcinoma	9/28/18	Regular	2018	The New England Journal of Medicine	70.67	6/4/18	No	Clinical outcomes only	85	1
6	NCT02578680	Gandhi L[6]	Pembrolizumab + pemetrexed + platinum	NSCLC	8/20/18	Regular	2018	The New England Journal of Medicine	70.67	4/16/18	No	Clinical outcomes only	616	72
7	NCT01928394	Ready N[7]	Nivolumab	SCLC	8/16/18	Accelerated	2018	Journal of Thoracic Oncology	12.4	10/10/18	No	Clinical outcomes only	109	112
8	NCT02060188	Overman MJ[8]	Ipilimumab + Nivolumab	Colorectral adenocarcinoma	7/10/18	Accelerated	2018	Journal of Clinical Oncology	28.35	01/20/18	Yes	Clinical outcomes and PRO results in the same manuscript	119	74
9	NCT02576990	Armand P[9]	Pembrolizumab	Large B-cell lymphoma	6/13/18	Accelerated	2018	Blood	16.6	11/21/18	No	Clinical outcomes only	53	72

10	NCT02628067	Chung HC[10]	Pembrolizumab	Cervical cancer	6/12/18	Regular	2018	Journal of Clinical Oncology	28.35	6/1/18	No	Clinical outcomes only	98	72
11	NCT02445248	Schuster SJ[11]	Tisagenlecleucel	Large B-cell lymphoma	5/1/18	Regular	2018	The New England Journal of Medicine	70.67	1/12/18	No	Clinical outcomes only	165	3
12	NCT02231749	Motzer RJ[12]	Ipilimumab + Nivolumab	Renal cell carcinoma	4/16/18	Regular	2018	The New England Journal of Medicine	70.67	4/5/18	Yes	PRO results in a secondary manuscript	1096	36
13	NCT02125461	Antonia SJ[13]	Durvalumab	NSCLC	2/16/18	Regular	2017	The New England Journal of Medicine	79.26	9/8/17	Yes	PRO results in a secondary manuscript	713	10
14	NCT02388906	Weber J[14]	Nivolumab	Melanoma	12/20/17	Regular	2017	The New England Journal of Medicine	79.26	9/10/17	Yes	Clinical outcomes and PRO results in the same	906	112

												manu script		
15	NCT02 348216	Neelapu S[15]	Axicabta gene ciloleucel	Large B-cell lympho ma	10/18/ 18	Regular	2017	The New Englan d Journa l of Medici ne	79.26	12/10/ 17	No	Clinic al outco mes only	109	0
16	NCT01 658878	El-Khoueiry AB[16]	Nivoluma b	Hepato cellular carcino ma	9/22/1 7	Acceler ated	2017	The Lancet	23.25	04/20/ 17	Yes	Clinic al outco mes and PRO results in the same manu script	262	112
17	NCT02 335411	Fuchs C[17]	Pembroli zumab	Gastric/ Gastro esopha geal junction adenoc arcino ma	9/22/1 7	Acceler ated	2018	JAMA Oncolo gy	22.4	5/10/1 8	No	Clinic al outco mes only	259	72
18	NCT02 435849	Maude SL[18]	Tisagenl ecleucel	Acute lympho blastic leukemi a	8/30/1 7	Regular	2018	The New Englan d Journa l of Medici ne	79.26	2/1/18	Yes	PRO results in a secon dary manu script	92	3
19	NCT02 060188	Overman M[19]	Nivoluma b	Colorec tral adenoc	7/31/1 7	Acceler ated	2017	The Lancet	36.42	7/19/1 7	Yes	Clinic al outco	74	112

				arcinoma				Oncology				mes and PRO results in the same manuscript		
20	NCT02256436	Bellmunt J[20]	Pembrolizumab	Urothelial carcinoma	5/18/17	Regular	2017	Journal of Clinical Oncology	26.36	2/17/17	Yes	PRO results in a secondary manuscript	542	72
21	NCT02039674	Langer C[21]	Pembrolizumab + pemetrexed + carboplatin	NSCLC	5/10/17	Accelerated	2016	The Lancet Oncology	33.9	10/10/16	No	Clinical outcomes only	123	72
22	NCT01772004	Patel MR[22]	Avelumab	Urothelial carcinoma	4/9/17	Accelerated	2017	The Lancet Oncology	36.42	12/5/17	No	Clinical outcomes only	249	8
23	NCT01693562	Powles T[23]	Durvalumab	Urothelial carcinoma	5/1/17	Accelerated	2017	JAMA Oncology	22.4	9/14/17	No	Clinical outcomes only	191	10
24	NCT02155647	Kaufman H[24]	Avelumab	Merkel cell carcinoma	4/23/17	Accelerated	2018	Journal for Immunotherapy of Cancer	8.3	1/19/18	Yes	PRO results in a secondary manuscript	88	8
25	NCT02453594	Chen R[25]	Pembrolizumab	Hodgkin	3/14/17	Accelerated	2017	Journal of	26.36	4/25/17	Yes	PRO results	210	72

				lymphoma				Clinical Oncology				in a secondary manuscript		
26	NCT02387996	Sharma P[26]	Nivolumab	Urothelial carcinoma	2/2/17	Accelerated	2017	The Lancet Oncology	36.42	1/26/17	No	Clinical outcomes only	270	112
27	NCT02105636	Ferris RL[27]	Nivolumab	SCCHN	11/10/16	Regular	2016	The New England Journal of Medicine	72.4	10/8/16	Yes	PRO results in a secondary manuscript	361	112
28-a*	NCT02142738	Reck M[28]	Pembrolizumab	NSCLC	10/24/16	Regular	2016	The New England Journal of Medicine	72.4	10/8/16	Yes	PRO results in a secondary manuscript	305	72
28-b*	NCT01905657	Herbst R[29]	Pembrolizumab	NSCLC	10/24/16	Regular	2015	The Lancet	47.8	12/19/15	Yes	PRO results in a secondary manuscript	1034	72
29-a†	NCT02008227	Rittmeyer A[30]	Atezolizumab	NSCLC	10/18/16	Regular	2016	The Lancet	47.8	12/13/16	Yes	PRO results in a secondary manuscript	850	18

29-b†	NCT01903993	Fehrenbacher L[31]	Atezolizumab	NSCLC	10/18/16	Regular	2016	The Lancet	47.8	3/10/16	No	Clinical outcomes only	287	18
30	NCT01848834	Mehra R[32]	Pembrolizumab	SCCHN	8/5/16	Accelerated	2018	British Journal of Cancer	5.4	6/29/18	No	Clinical outcomes only	192	72
31	NCT02108652.	Rosenberg JE[33]	Atezolizumab	Urothelial carcinoma	5/18/16	Accelerated	2016	The Lancet	47.8	3/6/16	No	Clinical outcomes only	311	18
32	NCT02181738	Younes A[34]	Nivolumab	Hodgkin lymphoma	5/17/16	Accelerated	2016	The Lancet Oncology	33.9	7/20/16	Yes	Clinical outcomes and PRO results in the same manuscript	80	113
33	NCT01668784	Motzer RJ[35]	Nivolumab	Renal cell carcinoma	11/23/15	Regular	2015	The New England Journal of Medicine	59.55	9/25/15	Yes	PRO results in a secondary manuscript	821	113
34	NCT00636168	Eggermont A[36]	Ipilimumab	Melanoma	10/28/15	Regular	2015	The Lancet Oncology	26.5	3/31/15	Yes	PRO results in a secondary	951	74

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35	NCT01673867	Borghaei H[37]	Nivolumab	NSCLC	10/9/15	Regular	2015	The New England Journal of Medicine	59.55	9/27/15	Yes	PRO results in a secondary manuscript	582	113
36	NCT01295827	Garon E[38]	Pembrolizumab	NSCLC	10/2/15	Accelerated	2015	The New England Journal of Medicine	59.55	4/19/15	No	Clinical outcomes only	495	72
37	NCT01927419	Postow MA[39]	Ipilimumab + Nivolumab	Melanoma	9/30/15	Accelerated	2015	The New England Journal of Medicine	59.55	4/20/15	No	Clinical outcomes only	142	113
38	NCT01642004	Brahmer J[40]	Nivolumab	NSCLC	03/04/2015	Regular	2015	The New England Journal of Medicine	59.55	5/31/15	Yes	PRO results in a secondary manuscript	272	113
39	NCT01721746	Weber J[41]	Nivolumab	Melanoma	12/22/14	Regular	2015	The Lancet Oncology	26.5	3/18/15	No	Clinical outcomes only	405	113

40	NCT02252042	Robert C[42]	Pembrolizumab	Melanoma	9/4/14	Accelerated	2014	The Lancet	45.2	7/15/14	No	Clinical outcomes only	173	72
41	NCT00006249	Eggermont A[43]	Peginterferon	Melanoma	3/29/11	Regular	2008	The Lancet	38.27	7/13/08	Yes	PRO results in a secondary manuscript	1256	199
42	NCT00094653	Hodi FS[44]	Ipilimumab	Melanoma	3/25/11	Regular	2010	The New England Journal of Medicine	53.29	6/5/10	Yes	PRO results in a secondary manuscript	676	1746

Information on PRO data														
ID	First author	PRO results publication date	Journal publishing the PRO results	Journal impact factor at time of publication	Endpoint	Hypothesis	PRO instruments	PRO instrument referenced	Primary statistical methods	Control for type I error	Clinical relevance definition	Approach for dealing with missing data	Study limitations	PRO conclusion[1]
8	Overman MJ[8]	01/20/2018	Journal of Clinical Oncology	28.35	Exploratory	No hypothesis reported	EORTC QLQ-C30, EQ-5D	Yes	Linear mixed effects model	Needed but not done	Change of X points	Reported	Not reported	Improvement in key PROs
12	Cella D[45]	1/15/19	The Lancet	35.38	Exploratory	Broad	EQ-5D, FACT-	Yes	Cox proportional	Needed but	Difference of	Reported	Reported	Experimental arm

			Oncology				G, FKSI-19		hazard/ Cox regression model, MMRM	not done	X points			is superior to control arm
13	Hui R[46]	10/7/2019	The Lancet	59.1	Secondary	Broad	EORTC QLQ-C30, EORTC QLQ-LC13, EQ-5D	Yes	Cox proportional hazard/ Cox regression model, Log-rank test, MMRM, Logistic regression	Needed and done	Change of X points	Reported	Reported	Similar outcomes between experimental arm and control arm
14	Weber J[14]	9/10/17	The New England Journal of Medicine	79.26	Secondary	No hypothesis reported	EORTC QLQ-C30, EQ-5D	Yes	Descriptive statistics	Needed but not done	Change of X points	Reported	Not reported	Similar outcomes between experimental arm and control arm
16	El-Khoueiry AB[16]	04/20/2017	The Lancet	23.25	Exploratory	No hypothesis reported	EQ-5D	Yes	Conventional wald method	Needed but not done	Not reported	Not reported	Not reported	Stable PROs
18	Laetsch T[47]	10/09/2019	The Lancet	59.1	Secondary	Broad	EQ-5D,	Yes	MMRM	Needed but	Difference of	Reported	Reported	Improvement in

							Peds QL			not done	X points			key PROs
19	Overman M[19]	7/19/17	The Lancet Oncology	36.42	Exploratory	No hypothesis reported	EORTC QLQ-C30, EQ-5D	Yes	Descriptive statistics	Needed but not done	Change of X points	Reported	Not reported	Improvement in key PROs
20	Vaughn D[48]	03/28/018	Journal of Clinical Oncology	26.36	Exploratory	Broad	EORTC QLQ-C30, EQ-5D	No	Cox proportional hazard/ Cox regression model, Log-rank test, Mixed effects model, cLDA/LDA	Needed but not done	Change of X points	Reported	Reported	Experimental arm is superior to control arm
24	Kaufman H[49]	08/12/2017	Future Oncology	2.36	Unclear	Broad	EQ-5D, FACT-M	Yes	Linear mixed effects model, Linear regression	Needed but not done	Not reported	Not reported	Reported	Improvement in key PROs
25	Tresckow B[50]	4/23/19	Leukemia & Lymphoma	2.64	Exploratory	Broad	EORTC QLQ-C30, EQ-5D	Yes	cLDA/LDA	Needed but not done	Change of X points	Reported	Reported	Improvement in key PROs
27	Harrington K[51]	6/23/17	The Lancet	36.4	Exploratory	Broad	EORTC QLQ-	Yes	Cox proportional	Needed but	Both	Reported	Reported	Experimental arm

			Oncology				C30, EORTC QLQ-H&N35, EQ-5D		hazard/ Cox regression model, ANCOVA, Brookmeyer and crowley	not done				is superior to control arm
28-a	Brahmer JR[52]	11/9/17	The Lancet Oncology	36.4	Exploratory	Broad	EORTC QLQ-C30, EORTC QLQ-LC13, EQ-5D	Yes	Cox proportional hazard/ Cox regression model, Log-rank test, cLDA/LDA	Needed but not done	Change of X points	Reported	Reported	Experimental arm is superior to control arm
28-b	Barlesi et al[53]	1/31/19	Journal of Thoracic Oncology	10.34	Exploratory	Broad	EORTC QLQ-C30, EORTC QLQ-LC13, EQ-5D	Yes	Cox proportional hazard/ Cox regression model, Log-rank test, Mixed effects model, cLDA/LDA	Needed but not done	Change of X points	Reported	Reported	Experimental arm is superior to control arm

29-a	Bordoni et al[54]	5/31/18	Clinical Lung Cancer	4.11	Secondary	Broad	EORTC QLQ-C30, EORTC QLQ-LC13	Yes	Cox proportional hazard/ Cox regression model, Log-rank test, ANCOVA	Needed but not done	Change of X points	Not reported	Reported	Experimental arm is superior to control arm
32	Younes A[34]	7/20/16	The Lancet Oncology	33.9	Exploratory	No hypothesis reported	EORTC QLQ-C30, EQ-5D	No	Descriptive statistics	Needed but not done	Not reported	Not reported	Not reported	Improvement in key PROs
33	Cella D[55]	6/6/16	The Lancet Oncology	33.9	Secondary	Broad	FKSI-DRS, EQ-5D	Yes	Cox proportional hazard/ Cox regression model, Mixed effects model, MMRM, Chi-squared test, t-tests	Needed but not done	Change of X points	Reported	Reported	Experimental arm is superior to control arm
34	Coens C[56]	11/10/17	The Lancet Oncology	26.5	Secondary	Specific	EORTC QLQ-C30	Yes	Linear mixed effects model	Needed and done	Change of X points	Reported	Reported	Experimental arm is inferio

														r to control arm
35	Reck M[57]	8/10/18	European Journal of Cancer	6.68	Secondary	Specific ‡	EQ-5D, LCSS	Yes	Cox proportional hazard/ Cox regression model, MMRM, t-tests, Clopper-pearson	Needed but not done	Both	Reported	Reported	Experimental arm is superior to control arm
38	Reck M[58]	11/10/17	Journal of Thoracic Oncology	10.34	Secondary	Specific ‡	EQ-5D, LCSS	Yes	Cox proportional hazard/ Cox regression model, MMRM, t-tests, Clopper-pearson	Needed but not done	Both	Reported	Reported	Experimental arm is superior to control arm
41	Bottomley A[59]	11/5/2009	Journal of Clinical Oncology	17.7	Secondary	Specific	EORTC QLQ-C30, IFN-specific symptom checklist	No	Cox proportional hazard/ Cox regression model, Log-rank test,	Needed and done	Change of X points	Reported	Reported	Experimental arm is inferior to control arm

									Linear mixed effects model, Logistic regression, Chi-squared test, Rank test					
42	Revicki D[60]	6/13/12	Health and Quality of Life Outcomes	2.27	Unclear	Broad	EORTC QLQ-C30	Yes	ANOVA	Needed but not done	Not reported	Reported	Reported	Similar outcomes between experimental arm and control arm

Abbreviations: NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; SCCHN, squamous cell carcinoma of the head and neck; PRO, patient reported outcomes; EQ-5D, EuroQol-5D; EORTC EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-core questionnaire; EORTC EORTC QLQ-LC13, EORTC EORTC QLQ-Lung Cancer Module; LCSS, Lung Cancer Symptom Scale; IFN, Interferon; FKSI-DRS, Functional Assessment of Cancer Therapy - Kidney Symptom Index - Disease related Symptoms; FACT-G, Functional Assessment of Cancer Therapy: General; FACT-M, FACT-Melanoma; PedsQL, Pediatric Quality of Life InventoryTM; MMRM, Mixed-model for repeated measures; LDA, longitudinal data analysis; cLDA, constrained LDA; ANOVA, analysis of variance; ANCOVA, analysis of covariance.
*Led to the same FDA approval
†Led to the same FDA approval
‡Found only in the protocol

Supplementary Table 3. Publishing PROs according to immunotherapy type, trial phase, randomization, approval type, cancer type

Variable	Published PRO data		p value
	Yes	No	
Immunotherapy type			0.5
Anti-PD1	12 (44)	15 (56)	
Anti-PDL1	3 (38)	5 (63)	
CAR-T	1 (33)	2 (68)	
Anti-CTLA4	2 (100)	0	
Anti-PD1 + Anti-CTLA4	2 (67)	1 (33)	
Interferon	1 (100)	0	
Clinical trial phase			0.012
Phase I	0	4 (100)	
Phase II	7 (33)	14 (67)	
Phase III	13 (77)	4 (24)	
Phase IV	1 (50)	1 (50)	
Randomization			0.68
Single-arm study	7 (33)	14 (67)	
Randomized trial	14 (61)	9 (39)	
Approval type			0.03
Regular	15 (63)	9 (38)	
Accelerated	6 (30)	14 (70)	
Cancer type			0.32
Non-small cell lung cancer	6 (50)	6 (50)	
Melanoma	4 (57)	3 (43)	
Urothelial carcinoma	1 (20)	4 (80)	
Large B-cell lymphoma	0	3 (100)	
Colorectral adenocarcinoma	2 (100)	0	
Hepatocellular carcinoma	1 (50)	1 (50)	
Hodgkin lymphoma	2 (100)	0	
Merkel cell carcinoma	1 (50)	1 (50)	

Renal cell carcinoma	2 (100)	0	
Squamous cell carcinoma of the head and neck	1 (50)	1 (50)	
Small cell lung cancer	0	1 (100)	
Gastric/gastroesophageal adenocarcinoma	0	1 (100)	
Cutaneous squamous cell carcinoma	0	1 (100)	
Cervical cancer	0	1 (100)	
Acute lymphoblastic leukemia	1 (100)	0	
Approval indication			0.25
First line	3 (33)	6 (67)	
Second line	10 (48)	11 (52)	
Third line or more	4 (40)	6 (60)	
Maintenance	1 (100)	0	
Adjuvant	3 (100)	0	
Primary endpoint			0.7
Included OS	10 (67)	5 (33)	
Did not include OS	11 (38)	18 (62)	

Abbreviations: PD1, programmed cell death 1; PDL1, PD-ligand 1; CAR-T, chimeric antigen receptor T; CTLA4, cytotoxic T lymphocyte associated protein 4; OS, overall survival
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Supplementary Table 4. Comparison of reporting characteristics between PROs published in a secondary dedicated manuscript (n=16) and those published in the primary manuscript only (n=5)

Variable	PRO in a secondary dedicated manuscript (n=16); N (%)	PRO in the primary manuscript only (n=5); N (%)	p value
Year of FDA approval			0·15
2008 - 2015	6 (38)	0	
2016 - 2018	10 (63)	5 (100)	
Randomized clinical trial			0·03
Yes	13 (81)	1 (20)	
No	3 (19)	4 (80)	
Specific PRO hypothesis	4 (25)	0	0·30
PRO endpoint			0·60
Secondary	8 (50)	1 (20)	
Exploratory	6 (38)	4 (80)	
Unclear	2 (13)	0	
Reference of the PRO instrument provided	14 (88)	4 (80)	0·58
PRO collection method reported	11 (69)	0	0·01
Site-specific PRO instrument	9 (56)	0	0·04
Control for type I error	3 (19)	0	0·42
Clinical relevance thresholds defined	14 (88)	3 (60)	0·23
Completion/compliance rate table provided	14 (88)	3 (60)	0·23
Strategy to deal with missing data defined	14 (88)	3 (60)	0·23
PRO specific study limitations reported	16 (100)	0	<0·0001
PRO data conclusion reported	16 (100)	5 (100)	1

Abbreviations: PRO, patient-reported outcomes; FDA, Food and Drug Administration. Numbers are rounded to the nearest whole number.