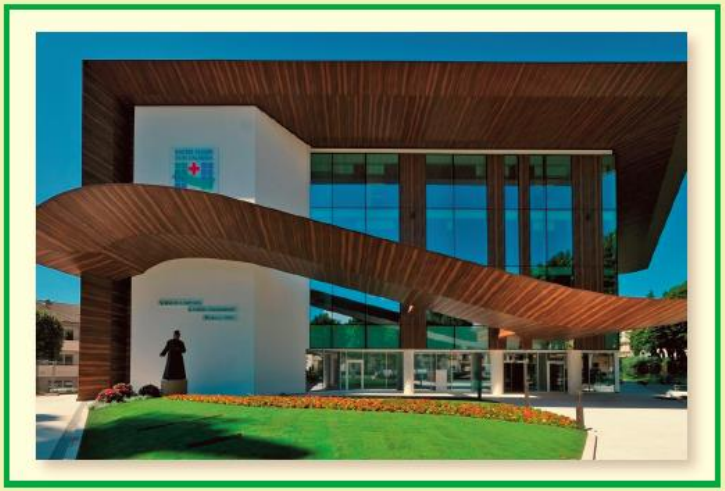
SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

SACRO CUORE DON CALABRIA IRCCS

1° Evento Alumni della Scuola



VENERDÌ 15 - SABATO 16 DICEMBRE 2023

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"
NEGRAR DI VALPOLICELLA (VR)

Patrocinio richiesti:

ALLEANZA CONTRO IL CANCRO - AICO - AIGOM - AIOM - AIRO
APS SENONETWORK ITALIA - ASSD - CIPOMO - FISM
ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
ISTITUTO SUPERIORE DI SANITÀ - ROPI - SIAPEC-IAP - SIF - SIPO - SIURO
SOCIETÀ ITALIANA DI CHIRURGIA - UNIVERSITÀ DI VERONA

Docenti

Rilievo (?) dei PROs
negli studi
for-profit e *non-profit*

Cosa ci hanno detto

- Cosa sono
- Quali sono
- Perche’ sono importanti
- Come si misurano
- Come si riportano
- Come si analizzano

Esistono differenze?

Critical Reviews in Oncology / Hematology 146 (2020) 102877

Contents lists available at ScienceDirect

Critical Reviews in Oncology / Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Quality of life assessment and reporting in colorectal cancer: A systematic review of phase III trials published between 2012 and 2018

Pasquale Lombardi[a], Laura Marandino[a], Emmanuele De Luca[b], Clizia Zichi[b], Maria Lu
Daniele Pignataro[c], Rosario F. Di Stefano[c], Eleonora Ghisoni[a], Annapaola Mariniello[c]
Elena Trevisi[c], Gianmarco Leone[c], Leonardo Muratori[c], Anna La Salvia[c,1], Cristina So
Francesco Leone[a,3], Massimo Aglietta[a], Silvia Novello[c], Giorgio V. Scagliotti[c], Francesc
Massimo Di Maio[b,*]

Review

Quality-of-Life Assessment and Reporting in Prostate Cancer: Systematic Review of Phase 3 Trials Testing Anticancer Drugs Published Between 2012 and 2018

Laura Marandino,[1] Emmanuele De Luca,[2] Clizia Zichi,[2] Pasquale Lombardi,[1]
Maria Lucia Reale,[3] Daniele Pignataro,[3] Rosario F. Di Stefano,[3] Eleonora Ghisoni,[1]
Annapaola Mariniello,[3] Elena Trevisi,[3] Gianmarco Leone,[3] Leonardo Muratori,[3]
ia,[3] Cristina Sonetto,[3] Consuelo Buttigliero,[3] Marcello Tucci,[3]
tta,[1] Silvia Novello,[3] Giorgio V. Scagliotti,[3] Francesco Perrone,[4]
Massimo Di Maio[2]

Lung Cancer 139 (2020) 47–54

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Quality of life analysis in lung cancer: A systematic review of phase III tri published between 2012 and 2018

Maria Lucia Reale[a], Emmanuele De Luca[b], Pasquale Lombardi[c], Laura Marandino[c], Clizia Zic
Daniele Pignataro[a], Eleonora Ghisoni[c], Rosario F. Di Stefano[a], Annapaola Mariniello[a],
Elena Trevisi[a], Gianmarco Leone[a], Leonardo Muratori[a], Anna La Salvia[a,1], Cristina Sonetto[a,
Paolo Bironzo[a], Massimo Aglietta[c], Silvia Novello[a], Giorgio V. Scagliotti[a], Francesco Perrone
Massimo Di Maio[b,*]

Critical Reviews in Oncology / Hematology 172 (2022) 103649

Contents lists available at ScienceDirect

Critical Reviews in Oncology / Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Inadequate health-related quality of life assessment and reporting in phase III clinical trials of immune checkpoint inhibitors in solid cancers: A systematic review

Alberto Servetto[a], Fabio Salomone[a], Fabrizio Di Costanzo[a], Rossella Iuliano[a],
Laura Marandino[b], Fabiana Napolitano[a], Antonio Santaniello[a], Pietro De Placido[a],
Sabino De Placido[a], Massimo Di Maio[c], Luigi Formisano[a,*], Roberto Bianco[a,*]

LUNG CANCER

Table 1
Characteristics of the 122 primary publications included in the analysis.

	N. publications	(%)
Year of primary manuscript		
2012	22	18.0%
2013	15	12.3%
2014	15	12.3%
2015	21	17.2%
2016	9	7.4%
2017	28	23.0%
2018	12	9.8%
Primary manuscript journal		
Journal of Clinical Oncology	38	31.1%
Lancet Oncology	31	25.4%
Annals of Oncology	18	14.8%
New England Journal of Medicine	16	13.1%
Lancet	5	4.1%
European Journal of Cancer	5	4.1%
Cancer	3	2.5%
British Journal of Cancer	2	1.6%
JAMA Oncology	2	1.6%
J Natl Cancer Inst	1	0.8%
JAMA	1	0.8%
Sources of funding		
Profit	80	65.6%
Non-profit	42	34.4%
Setting of disease		
NSCLC early stages – locally advanced	17	13.9%
NSCLC advanced / metastatic first line (incl. maintenance)	54	44.3%
NSCLC advanced / metastatic second / further lines	41	33.6%
SCLC (all stages and lines)	10	8.2%
Study design		
Superiority	115	94.3%
Non-inferiority	7	5.7%
Masking		
Open label	78	63.9%
Blinded	44	36.1%
Type of experimental therapy[a]		
Chemotherapy +/- other	63	51.6%
Targeted therapy +/- other	73	59.8%
Immunotherapy +/- other	22	18.0%
Other	4	3.3%
Primary endpoint		
Overall survival (alone or as co-primary)	68	55.7%
Other	54	44.3%
Study results (primary endpoint)		
Positive	54	44.3%
Negative	68	55.7%

Table 2
Inclusion of health-related quality of life among study endpoints according to characteristics of study and publication.

	Number of publications	QoL included among endpoints	QoL not included among endpoints
Whole series	122	83 (68.0%)	39 (32.0%)
Year of primary manuscript			
2012	22	15 (68.2%)	7 (31.8%)
2013	15	9 (60.0%)	6 (40.0%)
2014	15	13 (86.7%)	2 (13.3%)
2015	21	12 (57.1%)	9 (42.9%)
2016	9	7 (77.8%)	2 (22.2%)
2017	28	17 (60.7%)	11 (39.3%)
2018	12	10 (83.3%)	2 (16.7%)
Sources of funding			
Profit	80	64 (80.0%)	16 (20.0%)
Non-profit	42	19 (45.2%)	23 (54.8%)
Setting of disease			
NSCLC early stages – locally advanced	17	7 (41.2%)	10 (58.8%)
NSCLC advanced / metastatic first line (incl. maintenance)	54	39 (72.2%)	15 (27.8%)
NSCLC advanced / metastatic second / further lines	41	31 (75.6%)	10 (24.4%)
SCLC (all stages and lines)	10	6 (60.0%)	4 (40.0%)
Study design			
Superiority	115	77 (67.0%)	38 (33.0%)
Non-inferiority	7	6 (85.7%)	1 (14.3%)
Masking			
Open label	78	51 (65.4%)	27 (34.6%)
Blinded	44	32 (72.7%)	12 (27.3%)
Type of experimental therapy[a]			
Chemotherapy +/- other	63	42 (66.7%)	21 (33.3%)
Targeted therapy +/- other	73	52 (71.2%)	21 (28.8%)
Immunotherapy +/- other	22	17 (77.3%)	5 (22.7%)
Other	4	2 (50.0%)	2 (50.0%)
Primary endpoint			
Overall survival	68	46 (67.6%)	22 (32.4%)
Other	54	37 (68.5%)	17 (31.5%)
Study result			
Positive	54	42 (77.8%)	12 (22.2%)
Negative	68	41 (60.3%)	27 (39.7%)

[a] Categories are not mutually exclusive.

Perche’ dovrebbero esserci differenze?

Moda?

PubMed®

patient reported outcomes

Search

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RESULTS BY YEAR

134,845 results

Page 1 of 13,485

1966

2022: 18,474

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<< Prev Figure 3 Next >>

J Med Internet Res

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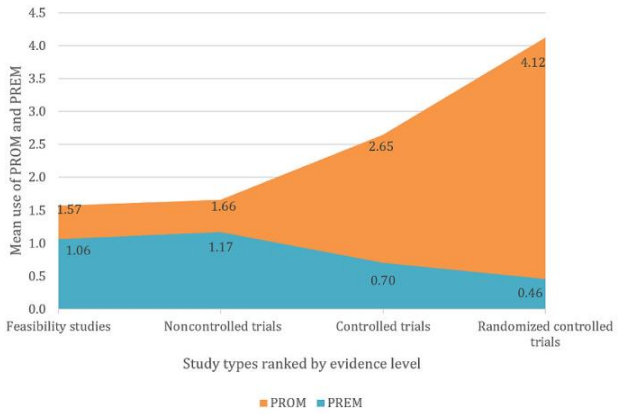
Figure 3



Use of patient-reported outcome measures and patient-reported experience measures by study type. PREM: patient-reported experience measure; PROM: patient-reported outcome measure.

Obbligatorietà?

In 2009, the US Food and Drug Administration (FDA) finalized a guidance for the inclusion of patient- reported outcomes (PROs) in clinical trials to sup- port the broader use of PROs in research across specialties.

Later in 2014, the European Medicines Agency (EMA) published a reflection paper on the inclusion of PROs in research. Nel 2020, l'EMA ha pubblicato la propria strategia denominata "*Regulatory Science Strategy to 2025*" (30), con l'obiettivo di favorire l'integrazione tra scienza e tecnologia nello sviluppo dei farmaci, di incentivare la qualità scientifica delle valutazioni, di promuovere terapie incentrate sul paziente in collaborazione con i sistemi sanitari e di affrontare le minacce sanitarie emergenti. In questo documento, l'agenzia rivela la propria volontà di sviluppare modalità sistematiche per incorporare gli esiti riportati dal paziente e le preferenze del paziente per la valutazione dei benefici e dei rischi delle terapie.

review articles

PATIENT CARE

Health-Related Quality of Life Data in Cancer Clinical Trials for Drug Registration: The Value Beyond Reimbursement

Erinne Wasalski, MSHS[1] and Shashi Mehta, PhD[2]

JCO Clin Cancer Inform 5:112-124. © 2021

Health-Related Quality of Life Data in Cancer Clinical Trials

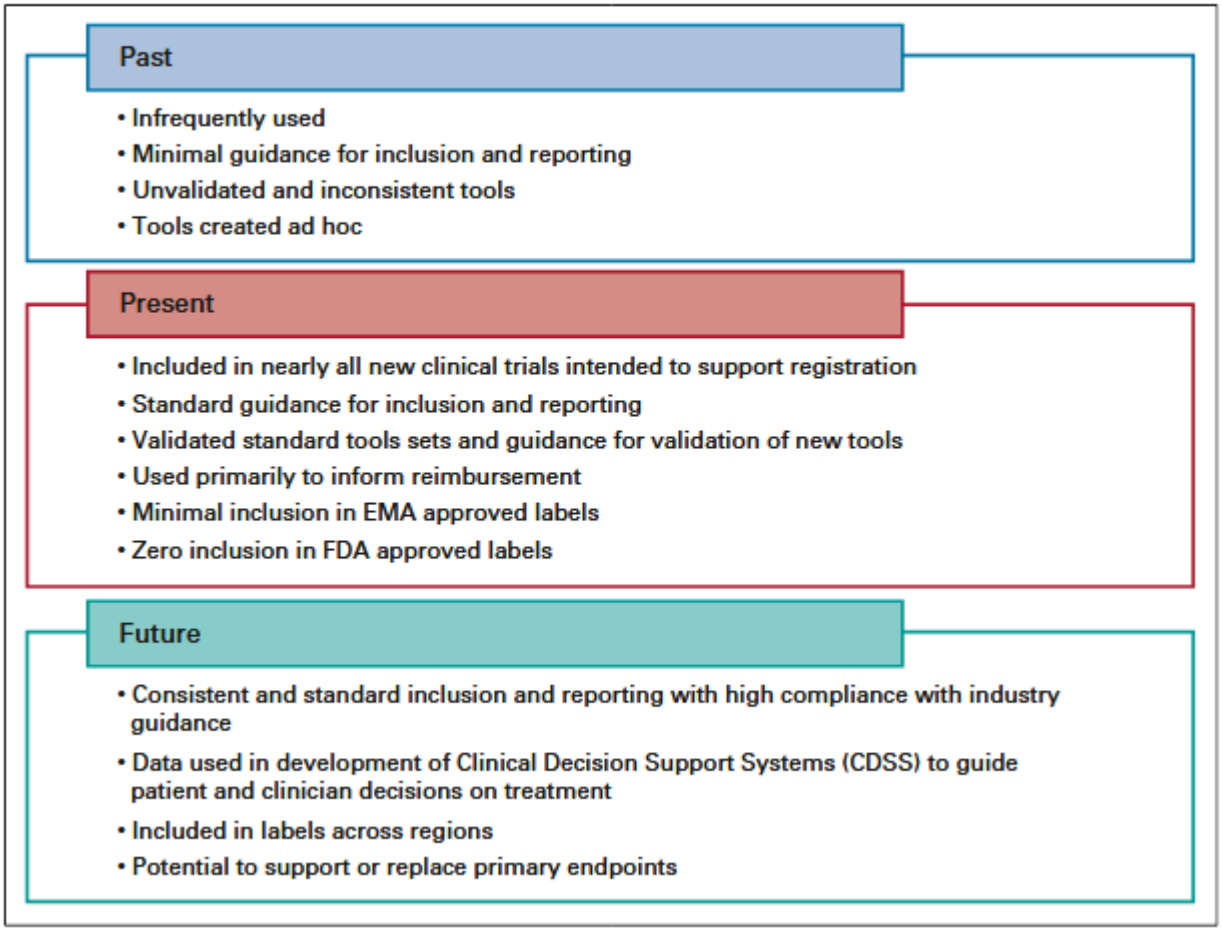


TABLE 4. Patient-Reported Outcome Data in Label Claims

Author (Year)	Focus	Years Reviewed; Focus	Author Conclusions
Gnanasakthy et al[54] (2012)	FDA approvals	2006-2010	18 oncology products reviewed zero included PRO label claims granted by the FDA
DeMuro et al[44] (2012)	FDA reasons for rejection of PRO label data	2006-2010	8 oncology compounds with data on rejected PRO label claims. 2 of the 8 did not include information related to reasons PRO data were rejected. Reasons for rejection of the other 6 included: • Fit for purpose • Study design, data quality, or interpretation • Administrative issues (such as tool not provided, provided tool not properly validated for the indication or use, or improper documentation) • No clinical benefit demonstrated.
DeMuro et al[45] (2013)	Differences between PRO data included in labels of dual-EMA/FDA approved compounds	2006-2010	14 compounds approved by the FDA with PRO label claims in compared to 35 approved by the EMA. None approved by the FDA were for oncology indications, whereas 6 of the EMA approved drugs with PRO data in the labels were for oncology indications.
Gnanasakthy et al[55] (2019)	Assessment of total EMA and FDA approvals of new oncology compounds	2012-2016	49 Oncology drugs with 64 unique indications approved by both the EMA and FDA. 45 included PRO data submitted in applications • 21 were approved by the EMA with PRO data in the labels • zero were approved by the FDA with PRO data in the labels.

Abbreviations: EMA, European Medicines Agency; FDA, (US) Food and Drug Administration; PRO, patient-reported outcome.

CONCLUSION

Despite available guidelines and the expectation from both the FDA and EMA to include PRO data in trials, only the EMA has approved PRO data to be included in labels

GRHTA | Glob Reg Health Technol Assess 2023; 10: 12-17
ISSN 2283-5733 | DOI: 10.33393/grhta.2023.2514
ORIGINAL RESEARCH ARTICLE

Il ruolo degli esiti riferiti dal paziente nelle decisioni di rimborso e innovatività dei farmaci in Italia

Francesco Malandrini[1], Cesare Borroni[2], Michela Meregaglia[1,2], Massimiliano Sarra[3], Oriana Ciani[1]

Questo lavoro analizza la presenza dei dati PROs/PROMs nel contesto dell'ammissione alla rimborsabilità e del Riconoscimento dell'innovatività a livello nazionale, mediante una revisione degli EPARs pubblicati dall'EMA e dei documenti prodotti a livello nazionale dall'AIFA nel quinquennio 2017-2021. Nello specifico, l'uso dei PROs/PROMs riscontrato negli EPARs (197 su 403, pari al 48,9%) è stato posto in relazione all'assegnazione delle classi di rimborsabilità e al riconoscimento dello status di innovatività da parte dell'AIFA. Dei 403 farmaci individuati nell'esame degli EPARs, l'attenzione si è focalizzata sui 229 (56,8%) che risultavano in commercio in Italia al momento dell'analisi, nello specifico 81 (35,4%) in classe A, 130 (56,7%) in classe H e 18 (7,9%) in classe C, di cui 113 (49,3%) riportavano l'uso di almeno un PRO/PROM.

TABELLA II - Uso dei PROs/PROMs per classi di rimborsabilità aifa (esclusi i farmaci in attesa/assenza di rimborso)

PRO/PROM	Classe A	Classe H	Classe C	Totale
Sì	37 (45,7%)	68 (52,3%)	8 (44,4%)	113 (49,3%)
No	44 (54,3%)	62 (47,7%)	10 (55,6%)	116 (50,7%)
Totale	81 (100%)	130 (100%)	18 (100%)	229 (100%)

Pearson Chi² (2) = 1,07 p = 0,59

TABELLA III - Uso dei PROs/PROMs in base allo stato di innovatività piena e condizionata

PRO/PROM	Innovativi	Non innovativi	Totale
Sì	33 (71,7%)	80 (43,7%)	113 (49,3%)
No	13 (28,3%)	103 (56,3%)	116 (50,7%)
Totale	46 (100%)	183 (100%)	229 (100%)

Pearson Chi² (1) = 11,55 p = **0,001**

PRO/PROM	Innovatività piena	Innovatività condizionata	Totale
Sì	21 (72,4%)	12 (70,6%)	33 (71,7%)
No	8 (27,6%)	5 (29,4%)	13 (28,3%)
Totale	29 (100%)	17 (100%)	46 (100%)

Pearson Chi² (1) = 0,02 p = 0,89

Tra i 46 farmaci innovativi, in realtà solo 9 (20%) riportano esplicitamente la considerazione di PROs/PROMs nelle schede di innovatività.

Risorse?

- Quali sono *diversi tipi di questionari, validati?
- Metodo di somministrazione *cartacei&web
- Come si misurano *misure ripetute
- Come si riportano *missing data
- Come si analizzano *missing data

An extract from MRC protocol LU20:
A named person in each centre must be nominated to take responsibility for the administration, collection and checking of the QoL forms. This may or may not be the clinician responsible for the patients.

NO EVIDENCE

Table 1 Characteristics of 72 Primary Publications

Characteristic	No. of Publications	% of Publications
Year of Primary Study		
2012	10	13.9
2013	11	15.3
2014	7	9.7
2015	11	15.3
2016	11	15.3
2017	13	18.1
2018	9	12.5
Journal Impact Factor		
Low (< 15)	21	29.2
Intermediate (15-30)	30	41.7
High (> 30)	21	29.2
Type of Sponsor		
For profit	37	51.4
Nonprofit	35	48.6
Setting of Disease		
Early stages	15	20.8
Advanced hormone sensitive (metastatic and biochemical relapse)	20	27.8
Castration resistant (metastatic and nonmetastatic)	37	51.4
Study Design		
Superiority	63	87.5
Noninferiority	9	12.5
Masking		
Open label	42	58.3
Blinded	30	41.7
Type of Experimental Therapy[a]		
Chemotherapy ± other	22	30.6
Targeted therapy ± other	11	15.3
Hormone therapy ± other	45	62.5
Immunotherapy ± other	4	5.6
Other	12	16.7
Primary End Point		
Overall survival	43	59.7
Other	29	40.3
Study Result		
Positive	34	47.2
Negative	38	52.8

PROSTATE CANCER

Bravura?
Risorse?
Adeguamento agenzie regolatorie?

NO EVIDENCE

COLORECTAL CANCER

Table 1
Characteristics of the 67 primary publications included in the analysis.

	Number of publications	(%)
Year of primary manuscript		
2012	9	13.4 %
2013	11	16.4 %
2014	7	10.5 %
2015	16	23.9 %
2016	9	13.4 %
2017	4	6,0 %
2018	11	16.4 %
Primary manuscript journal		
Annals of Oncology	18	26,8 %
British Journal of Cancer	2	3,0 %
European Journal of Cancer	4	6,0 %
JAMA	3	4.5 %
Journal of Clinical Oncology	14	20.9 %
Journal of National Cancer Institute	2	3,0 %
Lancet	2	3,0 %
Lancet Oncology	20	29,9 %
New England Journal of Medicine	2	3,0 %
Sources of funding		
Profit	26	38.8 %
Non-profit	41	61.2 %
Setting of disease		
Adjuvant/neoadjuvant setting	20	29.9 %
First-line or maintenance setting	26	38.8 %
Second and further lines	21	31.3 %
Study design		
Superiority	53	79,1 %
Non-inferiority	14	20.9 %
Masking		
Open label	52	77.6 %
Blinded	15	22.4 %
Countries involved		
Single country	33	49,3 %
2 or more countries	34	50.7 %
Type of experimental therapy[a]		
Chemotherapy +/- other	52	77.6 %
Targeted therapy +/- other	40	59,7 %
Primary endpoint		
Overall survival	21	31.3 %
Other	46	68.7 %
Study result		
Positive	32	47.8 %
Negative	35	52.2 %

[a] Categories are not mutually exclusive.

FUNDING EFFECT?

The term “funding effect” was formed in the 1980s, when it was discovered that researchers do not always report their results and conclusions honestly, but distort the findings to support the aims of the funding sources.[1] It has also shown that industry sponsored studies are more likely to publish positive results than those sponsored by not-for-profit and independent organisations.[1] One of the reasons is that funders may prevent publishing of the manuscript containing unfavourable results or even take some legal acts against researchers.[2] For example, in one case a sponsor sued a haematologist for breach of contract because she reported “concerns over the safety of a drug she was evaluating”.[3]

This distortion of reporting of the study results and conclusions occurs more often in studies funded by the pharmaceutical industry.[1] This can cause serious consequences because it directly affects the practice of medicine.[4] Nevertheless, every researcher with a funded study could be pressured to report results and conclusions that are more favourable to the funders, regardless of the topic or research area of the study.

BMJ

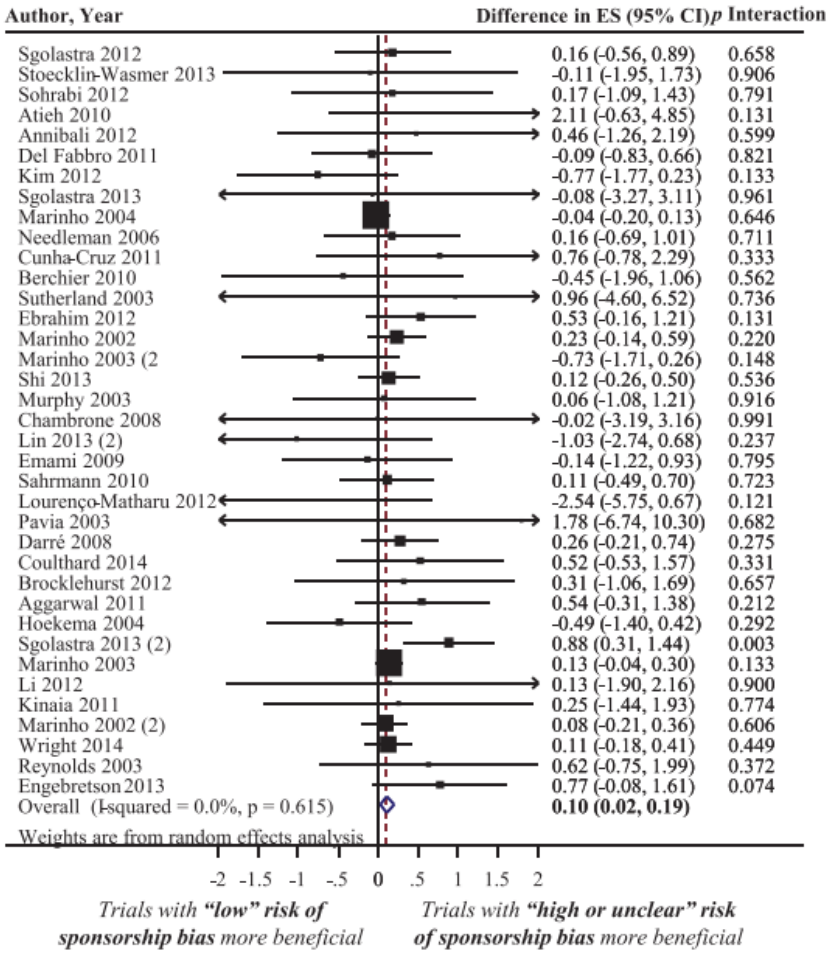
RESEARCH

Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study

Veronica Yank, clinical instructor,[1] Drummond Rennie, professor,[2] Lisa A Bero, professor[3]

Conclusion Meta-analyses on antihypertensive drugs and with financial ties to one drug company are not associated with favourable results but are associated with favourable conclusions.

Figure 1. Difference in treatment effect size (ES) estimate between trials with low and "high or unclear" risk of sponsorship bias. A positive value (more than 0) across meta-analyses indicates that trials with "high or unclear" risk of sponsorship bias exaggerate the ESs when compared with trials with "low" risk of sponsorship bias.



Interesse?

Health and Quality of Life Outcomes

BioMed Central

Commentary

Open Access

The FDA guidance for industry on PROs: the point of view of a pharmaceutical company

Fabio Arpinelli* and Francesco Bamfi

Address: Health Technology Assessment, Medical Department, GSK S.p.A. Verona, Italy

Email: Fabio Arpinelli* - fabio.a.arpinelli@gsk.com; Francesco Bamfi - francesco.a.bamfi@gsk.com

* Corresponding author

@The Patient-Reported Outcomes can provide additional data to make a drug more competitive than others of the same pharmacological class, and a well demonstrated positive impact on the patient' health status and daily life might allow a higher price and/or the inclusion in a reimbursement list.@

Critical Reviews in Oncology / Hematology 172 (2022) 103649

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journal homepage: www.elsevier.com/locate/critrevonc

Inadequate health-related quality of life assessment and reporting in phase III clinical trials of immune checkpoint inhibitors in solid cancers: A systematic review

Alberto Servetto [a], Fabio Salomone [a], Fabrizio Di Costanzo [a], Rossella Iuliano [a], Laura Marandino [b], Fabiana Napolitano [a], Antonio Santaniello [a], Pietro De Placido [a], Sabino De Placido [a], Massimo Di Maio [c], Luigi Formisano [a,*], Roberto Bianco [a,*]

Lancet	19	17.9
Lancet Oncology	21	19.8
New England Journal of Medicine	33	31.1
Control arm: placebo		
Yes	37	34.9
No	69	65.1
Immune checkpoint inhibitor in the experimental arm[a]		
Atezolizumab	20	18.9
Avelumab	8	7.6
Camrelizumab	3	2.8
Cemiplimab	1	0.9
Durvalumab	6	5.7
Ipilimumab	17	16.0
Nivolumab	26	24.5
Pembrolizumab	29	27.4
Sintilimab	3	2.8
Tislelizumab	1	0.9
Tremelimumab	6	5.7
Use of ICIs[b]		
Monotherapy	60	56.6
Plus chemotherapy	34	32.1
Plus target therapy	14	13.2
Plus immunotherapy	14	13.2
Plus other	2	1.9
Primary tumor		
Lung	35	33.0
Melanoma	15	14.2
Esophago-gastric	12	11.3
Kidney	8	7.6
Urothelial	8	7.6
Head-neck	6	5.7
Breast	6	5.7
Gynecological	5	4.7
Liver	3	2.8
Mesothelioma	3	2.8
Prostate	2	1.9
Colorectal	2	1.9
Brain	1	0.9
Disease setting		
Adjuvant/neoadjuvant	12	11.3
Metastatic	94	88.7
Funding		
Profit	103	97.2
Non-profit	3	2.8
Study design		
Superiority	105	99.1
Non-inferiority	1	0.9
Results of the trial		
Positive	74	69.8
Negative	32	30.2
Masking		
Blinded	40	37.8
Open label	66	62.2

European Journal of Cancer 195 (2023) 113404

Contents lists available at ScienceDirect

European Journal of Cancer

journal homepage: www.ejcancer.com

Systematic review and meta-analysis of immune checkpoint inhibitors as single agent or in combination with chemotherapy in early-stage non-small cell lung cancer: Impact of clinicopathological factors and indirect comparison between treatment strategies

Antonio Nuccio [a,b,1], Giuseppe Viscardi [c,1], Fabio Salomone [d], Alberto Servetto [d], Francesco Maria Venanzi [b], Silvia Teresa Riva [e], Sara Oresti [b], Francesca Rita Ogliari [b], Mariagrazia Viganò [b], Alessandra Bulotta [b], Robert Cameron [g], Alessandra Esposito [g], Jacobi Hines [g], Roberto Bianco [d], Michele Reni [a,b], Tina Cascone [f], Marina Chiara Garassino [g], Valter Torri [h], Giulia Veronesi [a,i], Michela Cinquini [h], Roberto Ferrara [a,b,*]

Critical Reviews in Oncology / Hematology 187 (2023) 104016

Contents lists available at ScienceDirect

Critical Reviews in Oncology / Hematology

journal homepage: www.elsevier.com/locate/critrevonc

A systematic review and meta-analysis on the optimal treatment duration of checkpoint inhibitoRS in solid tumors: The OTHERS study

Giorgio Bogani [a,*,1], Michela Cinquini [b,1], Diego Signorelli [c], Elio G. Pizzutilo [c,d], Rebecca Romanò [c,d], Melissa Bersanelli [e,f], Daniele Raggi [g], Salvatore Alfieri [h], Sebastiano Buti [e,f], Federica Bertolini [i], Pierluigi Bonomo [j], Laura Marandino [g], Mimma Rizzo [k], Marta Monteforte [b], Marco Aiello [l], Antonio C. Tralongo [b], Valter Torri [b], Violante Di Donato [a], Patrizia Giannatempo [g]

Patient or population: early resectable NSCLC

Intervention: neoadjuvant ICI + PCT

Comparison: neoadjuvant PCT

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with PCT	Risk with neoadjuvant ICI + PCT			
OS	Moderata		HR 0.66 (0.53 to 0.62) [death for any cause]	1645 (4 RCTs)	⨁⨁⨁⨁ High
	45 per 100	59 per 100 (61 to 65)			

ulation: radically resected NSCLC

Intervention: adjuvant ICI

Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	Risk with adjuvant			
OS	Low		HR 0.93 (0.78 to 1.11) [death for any cause]	2182 (2 RCTs)	⨁⨁⨁⨁ High
	22 per 100	24 per 100 (18 to 30)			

Study population: advanced/metastatic disease
Setting: inpatients
Intrevention: Immunotherapy until progression
Comparator: standard of care

Findings	Anticipated effect* (95% CI)		Relative effect (95% CI)	Number of partecipants (studies)	Level of evidence (GRADE)
	Risk for SoC until progression	Risk for immunotherapy until progression			
Overall Survival - NSCLC	62 per 100	53 per 100 (51 a 56)	HR 0.80 (0.74 a 0.87)	4595 (8 RCT)	⨁⨁⨁◯ Moderate[a]

Individuals: patients with advanced / metastatic solid tumors
Setting: inpatients
Intervention: Immunotherapy up to 2 years
Comparator: SoC

Findings	Anticipated effect* (95% CI)		Relative effects (95% CI)	Number of partecipants (studies)	Level of evidence (GRADE)
	Risk for SoC	Risk for immunotherapy up to 2 years			
Overall Survival - NSCLC	80 per 100	70 per 100 (67 a 72)	HR 0.73 (0.68 a 0.79)	4196 (6 RCT)	⨁⨁⨁⨁ High

SPECULAZIONE?