

Conclusions of clinical trials assessing monoclonal antibodies and sponsored by pharmaceutical industry: a meta-research study

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Supplementary material

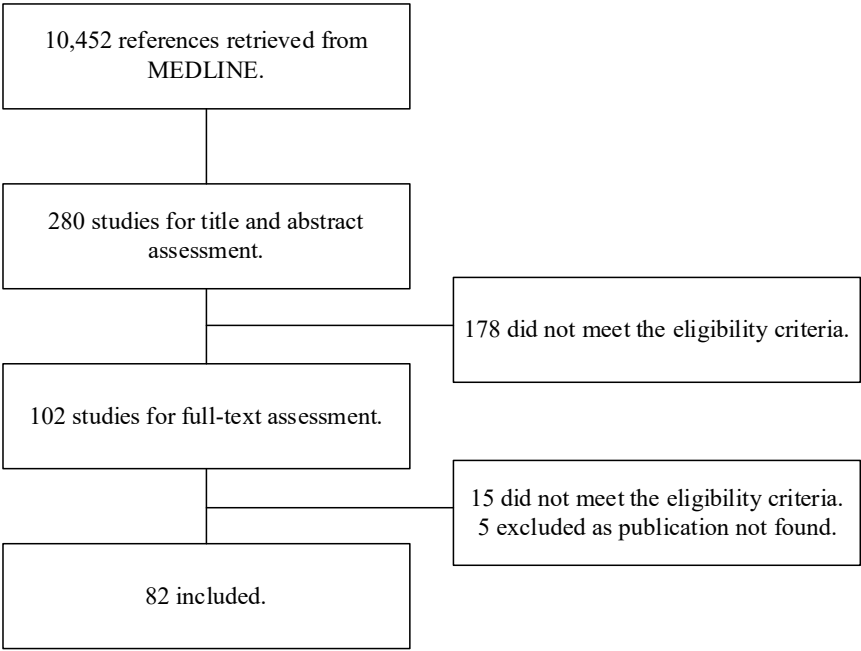
Supplementary file 1. Search strategy for MEDLINE (via PubMed)

#1 "Antibodies, Monoclonal"[Mesh] OR (Antibodies Monoclonal) OR (Monoclonal Antibodies) OR (Monoclonal Antibody) OR (Antibody, Monoclonal) OR (mAB)
#2 (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))
#3 1 AND #2

Supplementary file 2. Reasons for exclusions in the second phase of the selection process

	DOI	PMID	Reason for exclusion
1	10.1016/S2352-3026(22)00034-5	35240075	Intervention is not mab
2	10.1186/s10194-022-01387-y	35189811	Post hoc analysis
3	10.36849/jdd.6274	35133113	Not the main analysis – it is the extended phase analysis
4	10.1002/cpt.2539	35092305	Considered healthy participants
5	10.1007/s10147-021-02067-8	34973108	Post hoc analysis
6	10.1016/j.annonc.2021.12.002	34921960	Not the main analysis – it is the extended phase analysis
7	10.1172/JCI152670	34907910	Intervention is not mab
8	10.1007/s40121-021-00572-x	34878625	Considered healthy participants
9	10.3389/fimmu.2021.794638	34868084	Not funded by industry
10	10.1016/j.annonc.2021.11.009	34843940	Not randomized
11	10.1136/jitc-2021-002996	34815354	Not randomized
12	10.1016/S2468-1253(21)00298-3	34798039	No access to full text
13	10.1016/S2468-1253(21)00294-6	34798038	No access to full text
14	10.1016/S2468-1253(21)00295-8	34798037	No access to full text
15	10.1016/S2468-1253(21)00338-1	34798036	No access to full text
16	10.1038/s41392-021-00751-9	34650034	without comparison
17	10.1210/clinem/dgab729	34636899	Not the main analysis – it is the extended phase analysis
18	10.1016/S2468-1253(21)00313-7	34626550	No access to full text
19	10.1016/j.vaccine.2021.08.066	34483020	Considered healthy participants
20	10.1007/s00417-021-05281-2	34463842	Analysis isn't a RCT

56 **Supplementary file 3.** Flowchart of the selection process



57

Supplementary file 4. References included.

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Supplementary file 5. Characteristics of the publications that reported the controlled trials considered in this study.

	PMID	Publication (Author, year)	Clinical condition	Pharma Sponsor	Extent of funding (full/partial/unclear)	Pharma sponsor had data and publishing rights (y/n/nr)	Hypothesis (superiority, non-inferiority, equivalence, unclear)	Type of comparator (drug vs placebo, drug x vs drug y, drug vs similar, schedule a vs schedule b, drug vs procedure, drug + treatment x vs treatment x)	Direction of treatment effect to effectiveness (favorable, contrary, neutral)	Recommendation for clinical practice (y/n)	Recommendation direction for clinical practice (Totally favorable/Totally unfavorable/neutral)	Recognition of uncertainty (y/n)	Recognition of necessity or not of future studies (y/n)
1	35219277	Sivapalasingam 2022	COVID-19	regeneron pharmaceuticals, sanofi	partial	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
2	35218370	Lefferdink 2022	ichthyosis	Novartis	partial	y	superiority	drug vs placebo	Totally unfavorable	n	na	y	n
3	35194005	Hong 2021	lymphoma	Roche	full	y	superiority	drug x vs drug y	Totally favorable	y	Totally favorable	n	n
4	35179586	Mettu 2022	colorectal cancer	Roche	full	n	superiority	drug vs placebo	Totally favorable	n	na	n	n
5	35165274	Xu 2022	gastroesophageal cancer	innovent biologics, Eli Lilly	partial	y	superiority	drug x vs drug y	Totally favorable	y	Totally favorable	n	n
6	35139274	Schmid 2022	breast cancer	Merck	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	n
7	35139273	Tewari 2022	cervical cancer	regeneron pharmaceuticals, sanofi	full	y	superiority	drug x vs drug y	Totally favorable	y	Totally favorable	n	n
8	35133617	Li 2022	breast cancer	Pfizer	full	y	equivalence	drug vs similar	Totally favorable	y	Totally favorable	n	n
9	35130291	Samtsov 2022	psoriasis	JSC BIOCAD	full	y	equivalence	drug vs similar	Totally favorable	n	na	n	n
10	35108470	Doki 2022	gastroesophageal cancer	Bristol Myers Squibb, Ono Pharmaceutical	full	y	superiority	drug x vs drug y	Totally favorable	n	na	n	n

11	35106315	Lim 2021	influenza	Roche	full	y	superiority	drug vs placebo	Totally unfavorable	n	na	n	n
12	35105329	Stroyakovskiy 2022	lung cancer	JSC BIOCAD	full	y	equivalence	drug vs similar	Totally favorable	n	na	n	y
13	35104665	Chapurlat 2022	fibrous dysplasia of bone	Chugai Pharma	partial	n	superiority	drug vs placebo	Totally unfavorable	y	Totally unfavorable	y	y
14	35065057	Kaseb 2022	hepatocellular carcinoma	Bristol Myers Squibb	partial	n	superiority	drug x vs drug y	Totally favorable	n	na	n	y
15	35045221	Makker 2022	endometrial cancer	Eisai, Merck	full	y	superiority	drug x vs drug y	Totally favorable	n	na	n	n
16	35039035	Xu 2022	hypercholesterolemia	Jiangsu Hengrui Medicine Co.	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	y
17	35038433	Safran 2022	gastroesophageal cancer	roche	partial	n	superiority	drug + treatment x vs treatment x	Totally unfavorable	n	na	n	y
18	35032437	Cella 2022	renal cancer	Bristol Myers Squibb, Ono Pharmaceutical, Exelixis, Ipsen Pharma, Takeda Pharmaceutical	full	y	superiority	drug x vs drug y	Totally favorable	n	na	n	n
19	35030335	Kang 2022	gastroesophageal cancer	Ono Pharmaceutical, Bristol-Myers Squibb	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
20	35029629	O'Brien 2022	COVID-19	regeneron pharmaceuticals, roche	partial	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
21	35026342	Zhang 2022	psoriasis	Jiangsu Hengrui Medicine Co.	full	y	superiority	drug vs placebo	Totally favorable	n	na	y	y
22	35013615	Powles 2022	prostate cancer	roche	full	y	superiority	drug + treatment x vs treatment x	Totally unfavorable	n	na	n	y
23	34986285	Tawbi 2022	melanoma	Bristol Myers Squibb	full	y	superiority	drug + treatment x	Totally favorable	n	na	n	n

								vs treatment x					
24	34981077	Chew 2021	COVID-19	Eli Lilly	partial	n	superiority	drug vs placebo	Totally favorable	n	na	y	y
25	34936739	Bachelez 2021	psoriasis	Boehringer Ingelheim	full	y	superiority	drug vs placebo	Totally favorable	n	na	y	y
26	34920291	Ledermann 2022	ovarian cancer	Glycotope GmbH	full	n	superiority	drug vs placebo	Totally unfavorable	n	na	n	y
27	34914889	Yau 2022	hepatocellular carcinoma	Bristol Myers Squibb, Ono Pharmaceutic al	full	y	superiority	drug x vs drug y	Totally favorable	y	Totally favorable	n	n
28	34911706	Kristensen 2021	psoriatic arthritis	AbbVie	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	n
29	34904799	Tilly 2021	lymphoma	roche	full	y	superiority	drug x vs drug y	Totally favorable	n	na	n	n
30	34893523	Shah 2021	gastroesopha geal cancer	Gilead Sciences	full	n	superiority	drug + treatment x vs treatment x	Totally unfavorable	n	na	n	n
31	34890214	Krop 2021	breast cancer	Roche	full	y	superiority	drug x vs drug y	Totally unfavorable	n	na	n	n
32	34879449	Bacharier 2021	asthma	sanofi, regeneron pharmaceutic als	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
33	34878659	Chung 2021	gastroesopha geal cancer	Merck	full	y	superiority	drug x vs drug y	neutral	n	na	y	y
34	34871550	Usmani 2021	multiple myeloma	Amgen, Janssen	full	y	superiority	drug + treatment x vs treatment x	Totally favorable	y	Totally favorable	n	n
35	34871182	Perlin 2022	COVID-19	Avalo Therapeutics	full	n	superiority	drug vs placebo	Totally favorable	n	na	y	y
36	34863332	Temesgen 2021	COVID-19	humanigen	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
37	34861168	Bowman 2022	Sjögren's syndrome	Novartis	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	y
38	34839016	Soo 2022	lung cancer	AstraZeneca, Roche	partial	n	superiority	drug + treatment x vs treatment x	Totally unfavorable	n	na	n	n

39	34818112	Wolchok 2022	melanoma	Bristol Myers Squibb	full	y	superiority	drug x vs drug y	Totally favorable	n	na	n	n
40	34816373	Cai 2021	psoriasis	Shanghai Henlius Biotech	full	y	equivalence	drug vs similar	Totally favorable	y	Totally favorable	n	n
41	34806021	Bauer 2021	septic shock	InflaRx GmbH	full	n	superiority	drug vs placebo	Totally favorable	n	na	n	y
42	34786956	Konno 2021	chronic low back pain	Pfizer, Eli Lilly	full	y	not reported	drug x vs drug y	Totally favorable	n	na	y	y
43	34748774	Sands 2021	Crohn's Disease	Eli Lilly	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
44	34744750	Dai 2021	low bone mass	Jiangsu Hengrui Pharmaceuticals	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	y
45	34719872	McInnes 2022	psoriatic arthritis	Janssen	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
46	34716979	Shoji 2021	ovarian cancer	Chugai Pharmaceutical	full	y	superiority	drug + treatment x vs treatment x	Totally favorable	n	na	n	y
47	34706556	Ruff 2021	Coronary Artery Disease	AstraZeneca	full	n	superiority	drug vs placebo	Totally favorable	n	na	n	y
48	34706311	Gaffo 2021	gout	Amgen	full	n	superiority	drug + treatment x vs treatment x	Totally unfavorable	y	Totally unfavorable	n	n
49	34706189	Gupta 2021	COVID-19	Vir Biotechnology, GlaxoSmithKline	full	n	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	y
50	34706172	Brightling 2021	asthma	AbbVie, Boehringer Ingelheim	full	n	superiority	drug vs placebo	Totally unfavorable	n	na	n	n
51	34706171	Wechsler 2021	asthma	Sanofi, Regeneron Pharmaceuticals	full	n	superiority	drug vs placebo	Totally favorable	n	na	n	n
52	34657274	Feldman 2021	psoriasis	Alvotech Swiss AG	full	y	equivalence	drug vs similar	Totally favorable	y	Totally favorable	n	n
53	34656227	Fennell 2021	mesothelioma	Bristol Myers Squibb	partial	n	superiority	drug vs placebo	Totally favorable	n	na	n	n

54	34655533	Facon 2021	multiple myeloma	Janssen	full	y	superiority	drug + treatment x vs treatment x	Totally favorable	y	Totally favorable	n	n
55	34650833	Hasanov 2021	melanoma	Prometheus Laboratories, Clinigen	full	y	superiority	schedule a vs schedule b	Totally favorable	n	na	n	n
56	34642026	Konecny 2021	ovarian cancer	amgen	partial	n	superiority	drug vs placebo	Totally unfavorable	n	na	n	y
57	34615636	Furie 2021	lupus nephritis	Roche	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	y
58	34609549	Rosas 2021	COVID-19	Roche	full	y	superiority	drug vs placebo	Totally unfavorable	n	na	n	n
59	34607285	Reck 2021	lung cancer	Bristol Myers Squibb	full	y	superiority	schedule a vs schedule b	Totally favorable	y	Totally favorable	n	n
60	34605947	Laterre 2021	septic shock	Adrenomed AG	full	not reported	superiority	drug vs placebo	Totally favorable	n	na	n	y
61	34599540	Sweet 2021	lung transplant recipient	Roche	partial	n	superiority	drug vs placebo	Totally favorable	n	na	n	y
62	34592180	Valle 2021	biliary tract cancer	Eli Lilly	full	y	superiority	drug vs placebo	Totally unfavorable	n	na	n	n
63	34587383	Weinreich 2021	COVID-19	Regeneron Pharmaceuticals, Roche	partial	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
64	34586459	Lomakin 2021	COVID-19	JSC BIOCAD	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	n
65	34563243	Fleischmann 2021	rheumatoid arthritis	pfiizer	full	y	equivalence	drug vs similar	Totally favorable	n	na	n	n
66	34548479	Keenan 2021	breast cancer	Merck, Eisai	partial	n	superiority	drug + treatment x vs treatment x	Totally favorable	n	na	y	y
67	34548383	Briot 2021	X-linked hypophosphatemia	Kyowa Kirin International	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	n
68	34543477	Satouchi 2021	lung cancer	Merck	full	y	superiority	drug x vs drug y	Totally favorable	y	Totally favorable	n	n
69	34537057	Rigby 2021	rheumatoid arthritis	Bristol Myers Squibb	full	y	superiority	drug x vs drug y	Totally unfavorable	n	na	y	y
70	34534429	Colombo 2021	cervical cancer	Merck	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n

71	34533973	Modest 2022	colorectal cancer	Amgen	partial	n	superiority	drug + treatment x vs treatment x	Totally favorable	y	Totally favorable	n	y
72	34529931	Moreau 2021	multiple myeloma	Janssen	partial	n	superiority	drug + treatment x vs treatment x	Totally favorable	n	na	n	y
73	34521687	French 2021	Epilepsy	biogen	full	y	superiority	drug vs placebo	Totally unfavorable	n	na	y	y
74	34519801	Luo 2021	gastroesophageal cancer	Jiangsu Hengrui Pharmaceuticals	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	n
75	34507350	Horwitz 2021	lymphoma	Takeda Development Center Americas	unclear	nr	superiority	drug x vs drug y	Totally favorable	n	na	n	n
76	34499874	Pinto 2021	mesothelioma	Eli Lilly	full	n	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	y
77	34482179	Klinghammer 2021	cancer of the head and neck	Glycotope	full	y	superiority	drug x vs drug y	Totally unfavorable	n	na	n	y
78	34477816	Buske 2021	lymphoma	Celltrion	full	y	equivalence	drug vs similar	Totally favorable	n	na	n	n
79	34473544	Hamanishi 2021	ovarian cancer	Ono Pharmaceutical, Bristol-Myers Squibb	full	y	superiority	drug x vs drug y	Totally unfavorable	n	na	n	n
80	34462864	Paller 2021	Atopic Dermatitis	Sanofi, Regeneron Pharmaceuticals	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	n
81	34455583	Chen 2021	COVID-19	Eli Lilly	full	y	superiority	drug vs placebo	Totally favorable	n	na	n	y
82	34454674	Sun 2021	gastroesophageal cancer	Merck	full	y	superiority	drug vs placebo	Totally favorable	y	Totally favorable	n	n

N = No NA = Not Applicable N=No NR = Not Reported Y = Yes

Supplementary file 6. Clinical Conditions grouped according to ICD-10

Chapter ICD-10	Categorie ICD-10	Clinical Condition	Number of studies (n=82)	Percentage
Diseases of the respiratory system	Chronic lower respiratory diseases	Asthma	3	3,7
Diseases of the skin and subcutaneous tissue	Dermatitis and eczema	Atopic dermatitis	1	1,2
Diseases of the musculoskeletal system and connective tissue	Disorders of bone density and structure	Low bone mass	1	1,2
Diseases of the nervous system	Episodic and paroxysmal disorders	Epilepsy	1	1,2
Diseases of the genitourinary system	Glomerular diseases	Lupus nephritis	1	1,2
Diseases of the musculoskeletal system and connective tissue	Inflammatory polyarthropathies	Rheumatoid arthritis	2	2,4
		Gout	1	1,2
		Psoriatic arthritis	2	2,4
Diseases of the respiratory system	Influenza and pneumonia	Influenza	1	1,2
Diseases of the circulatory system	Ischaemic heart diseases	Coronary artery disease	1	1,2
Neoplasms	Malignant neoplasm of breast	Breast cancer	4	4,9
	Malignant neoplasms of digestive organs	Biliary tract cancer	1	1,2
		Colorectal cancer	2	2,4
		Gastroesophageal cancer	8	9,8
		Hepatocellular carcinoma	2	2,4
	Malignant neoplasms of female genital organs	Cervical cancer	2	2,4
		Ovarian cancer	4	4,9
		Endometrial cancer	1	1,2
	Malignant neoplasms of ill-defined, secondary and unspecified sites	Head and neck cancer	1	1,2
	Malignant neoplasms of male genital organs	Prostate cancer	1	1,2
	Malignant neoplasms of respiratory and intrathoracic organs	Lung cancer	4	4,9
		Mesothelioma	2	2,4
	Malignant neoplasms of urinary tract	Renal cancer	1	1,2

	Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	Lymphoma	4	4,9
		Multiple myeloma	3	3,7
		Melanoma and other malignant neoplasms of skin	Melanoma	3
Endocrine, nutritional and metabolic diseases	Metabolic disorders	Hypercholesterolemia	1	1,2
		X-linked hypophosphataemia	1	1,2
Diseases of the digestive system	Noninfective enteritis and colitis	Crohn’s Disease	1	1,2
Diseases of the musculoskeletal system and connective tissue	Osteopathies and chondropathies	Fibrous dysplasia of bone	1	1,2
Certain infectious and parasitic diseases	Other bacterial diseases	Septic shock	2	2,4
Congenital malformations, deformations and chromosomal abnormalities	Other congenital malformations	Ichthyosis	1	1,2
Diseases of the musculoskeletal system and connective tissue	Other dorsopathies	Chronic low back pain	1	1,2
Certain infectious and parasitic diseases	Other viral diseases	COVID-19	10	12,2
Diseases of the skin and subcutaneous tissue	Papulosquamous disorders	Psoriasis	5	6,1
Factors influencing health status and contact with health services	Persons with potential health hazards related to family and personal history and certain conditions influencing health status	Lung transplant recipient	1	1,2
Diseases of the musculoskeletal system and connective tissue	Systemic connective tissue disorders	Sjogren’s syndrome	1	1,2

Supplementary file 7. List of pharmaceutical industries sponsors

Pharma sponsor	Studies sponsored	% of included studies (n=82)
Roche	15	18,3%
Bristol Myers Squibb	11	13,4%
Lilly	7	8,5%
Merck	7	8,5%
regeneron pharmaceuticals	7	8,5%
Ono Pharmaceutical	5	6,1%
sanofi	5	6,1%
Amgen	4	4,9%
Janssen	4	4,9%
Jiangsu Hengrui	4	4,9%
JSC BIOCAD	3	3,7%
Pfizer	3	3,7%
AbbVie	2	2,4%
AstraZeneca	2	2,4%
Boehringer Ingelheim	2	2,4%
Eisai	2	2,4%
Glycotope GmbH	2	2,4%
Novartis	2	2,4%
Takeda	2	2,4%
Adrenomed AG	1	1,2%
Alvotect Swiss AG	1	1,2%
Avalo Therapeutics	1	1,2%
biogen	1	1,2%
Celltrion	1	1,2%
Clinigen	1	1,2%
Exelixis	1	1,2%
Gilead Sciences	1	1,2%
GlaxoSmithKline	1	1,2%
humanigen	1	1,2%
InflaRx	1	1,2%
innovent bio	1	1,2%
Ipsen Pharma	1	1,2%
Kyowa Kirin International	1	1,2%
Prometheus Laboratories	1	1,2%
Shanghai Henlius Biotech	1	1,2%
Vir Biotechnology	1	1,2%