Supporting Information

Efficacy and safety of multiple Dupilumab dose regimens in patients with moderate-to-

severe atopic dermatitis: A systematic review and network meta-analysis of randomized

controlled trials

Supplementary Contents

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Fig. S1. Forest plots of pairwise meta-analyses and network meta-analyses of efficacy. Outcomes: (a) EASI-50; (b) IGA score 0 or 1 (c) Peak pruritus NRS score, improvement \geq 3 points

Fig. S2. Forest plots of pairwise meta-analyses and network meta-analyses of safety. Outcomes: (a) ≥ 1 AEs; (b) ≥ 1 SAEs

Table S1. PRISMA extension for NMA 2015 checklist.

Section/Topic	ltem #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review incorporating a network meta-analysis (or related form of meta-analysis).	1
ABSTRACT			
Structured summary	2	 Provide a structured summary including, as applicable: Background: main objectives Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and synthesis methods, such as network meta-analysis. Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity. Discussion/Conclusions: limitations; conclusions and implications of findings. Other: primary source of funding; systematic review registration number with registry name. 	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, including mention of why a network meta-analysis has been conducted.	4-5
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web	6

registration		address); and, if available, provide registration information, including registration number.				
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. Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).	6			
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.	6			
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6			
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).				
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.				
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7			
Geometry of the network	S1	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	8-9			
Risk of bias within 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.	8			
Summary measures	Summary State the principal summary measures (e.g., risk ratio, difference in means). Also describe the use 13 13					

		cumulative ranking curve (SUCRA) values, as well as modified approaches used to present				
		summary findings from meta-analyses.				
		Describe the methods of handling data and combining results of studies for each network meta-				
Planned methods		analysis. This should include, but not be limited to:				
	14	Handling of multi-arm trials;	8-9			
of analysis		Selection of variance structure;				
		• Selection of prior distributions in Bayesian analyses; and Assessment of model fit.				
Assessment of	S2	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence				
Inconsistency	52	in the treatment network(s) studied. Describe efforts taken to address its presence when found.	9			
Risk of bias across	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication	8-9			
studies	15	bias, selective reporting within studies).				
		Describe methods of additional analyses if done, indicating which were pre-specified. This may				
		include, but not be limited to, the following:				
		 Sensitivity or subgroup analyses; 	Ness			
Additional analyses	16	Meta-regression analyses;	None			
		Alternative formulations of the treatment network; and				
		• Use of alternative prior distributions for Bayesian analyses (if applicable).				
RESULTS [†]						
Church and a string of	47	Give numbers of studies screened, assessed for eligibility, and included in the review, with	9-10			
Study selection	17	reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1			
Presentation of	62	Provide a network graph of the included studies to enable visualization of the geometry of the	10-11			
network structure	S3	treatment network.	Figure 3			
Summary of	64	Provide a brief overview of characteristics of the treatment network. This may include	10.11			
network geometry	S4	commentary on the abundance of trials and randomized patients for the different interventions	10-11			

		and pairwise comparisons in the network, gaps of evidence in the treatment network, and	
		potential biases reflected by the network structure.	
Study	4.0	For each study, present characteristics for which data were extracted (e.g., study size, PICOS,	10
characteristics	18	follow-up period) and provide the citations.	Table 1
Risk of bias within	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	10
studies	15		Figure 2
Results of		For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data	11-12
individual studies	20	for each intervention group, and 2) effect estimates and confidence intervals. Modified	Tables 2-4
individual studies		approaches may be needed to deal with information from larger networks.	Figure 4
		Present results of each meta-analysis done, including confidence/credible intervals. In larger	
		networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or	
Synthesis of results	21	standard care), with full findings presented in an appendix. League tables and forest plots may be	Figure 5
		considered to summarize pairwise comparisons. If additional summary measures were explored	
		(such as treatment rankings), these should also be presented.	
Fundamentian for		Describe results from investigations of inconsistency. This may include such information as	12-13
Exploration for	S 5	measures of model fit to compare consistency and inconsistency models, P values from statistical	Tables
inconsistency		tests, or summary of inconsistency estimates from different parts of the treatment network.	S2-6
Risk of bias across	22	Present results of any assessment of risk of bias across studies for the evidence base being	Tables
studies	22	studied.	S2-6
Desults of		Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression	
Results of	23	analyses, alternative network geometries studied, alternative choice of prior distributions for	None
additional analyses		Bayesian analyses, and so forth).	
DISCUSSION			

Summary of	24	Summarize the main findings, including the strength of evidence for each main outcome;	13-15
evidence		consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	
		Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g.,	
Limitations	25	incomplete retrieval of identified research, reporting bias). Comment on the validity of the	15-16
Linitations	25	assumptions, such as transitivity and consistency. Comment on any concerns regarding network	15-10
		geometry (e.g., avoidance of certain comparisons).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications	16
Conclusions	20	for future research.	10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data);	Nono
Funding	27	role of funders for the systematic review.	None
PICOS = population	, inter	vention, comparators, outcomes, study design.	
* Text in italics indi	cate S	wording specific to reporting of network meta-analyses that has been added to guida	nce from
the PRISMA statem	ent.		
+ Authors may wish	n to pla	an for use of appendices to present all relevant information in full detail for items in th	nis
section.			

Table S2. Assessment of inconsistency in all studies. Outcome: EASI-50

Comparison	Number	Network meta-	Direct	Indirect	Difference of direct and	Lower limit of	Upper limit of	P value
	of studies	analysis	comparison	comparison	indirect comparison	95% CI	95% CI	
100mg QM: 200mg Q2W	1	-0.3807854	-0.3338037	-0.6113816	0.27757787	-0.6275386	1.18269434	0.54779023
100mg QM: 300mg Q2M	0	-0.2326956	-	-0.2326956	-	-	-	-
100mg QM: 300mg Q2W	1	-0.596285	-0.5602314	-0.8213851	0.26115377	-0.6608148	1.18312236	0.57877639
100mg QM: 300mg QM	1	-0.4254806	-0.4613456	-0.1942985	-0.267047	-1.2316197	0.69752562	0.58738707
100mg QM: 300mg QW	1	-0.5616805	-0.6152004	-0.1428069	-0.4723935	-1.4730452	0.52825817	0.35482479
100mg QM: Placebo	1	0.27077862	0.41341067	0.16675228	0.24665838	-0.4121548	0.90547158	0.46306655
200mg Q2W: 300mg Q2M	0	0.14808979	-	0.14808979	-	-	-	-
200mg Q2W: 300mg Q2W	1	-0.2154996	-0.2264276	-0.2061406	-0.020287	-0.4106922	0.37011815	0.9188776
200mg Q2W: 300mg QM	2	-0.0446951	-0.0471556	0.00553513	-0.0526908	-0.8647944	0.75941281	0.89880897
200mg Q2W: 300mg QW	1	-0.1808951	-0.2813967	-0.0889107	-0.192486	-0.5794771	0.19450517	0.32962535
200mg Q2W: Placebo	2	0.65156405	0.70734133	0.59756506	0.10977627	-0.2773749	0.49692746	0.57838484
300mg Q2M: 300mg Q2W	0	-0.3635894	-	-0.3635894	-	-	-	-
300mg Q2M: 300mg QM	1	-0.1927849	-0.0990718	-0.8778625	0.77879072	-0.1058206	1.66340203	0.0844364
300mg Q2M: 300mg QW	0	-0.3289849	-	-0.3289849	-	-	-	-
300mg Q2M: Placebo	1	0.50347426	0.32015764	0.89128836	-0.5711307	-1.2198656	0.07760415	0.0844364
300mg Q2W: 300mg QM	1	0.17080447	0.0988858	0.22524412	-0.1263583	-0.4730138	0.2202971	0.47496716
300mg Q2W: 300mg QW	5	0.03460451	0.03244257	2.05733268	-2.0248901	-4.9215316	0.8717514	0.17065319
300mg Q2W: Placebo	5	0.86706365	0.8737915	0.81821199	0.05557951	-0.3234827	0.43464168	0.77382349
300mg QM: 300mg QW	1	-0.1362	-0.1538549	-0.1217964	-0.0320584	-0.3742588	0.31014195	0.85431496
300mg QM: Placebo	4	0.69625917	0.72400504	0.64170415	0.08230089	-0.268446	0.43304782	0.64559156
300mg QW: Placebo	5	0.83245914	0.83131447	0.84093234	-0.0096179	-0.3869156	0.36767985	0.96015241
"-" means data not app	licable. EAS	SI, Eczema Area S	everity Index.	•				

Table S3. Assessment of inconsistency in all studies. Outcome: IGA score 0 or 1

Comparison	Number	Network meta-	Direct	Indirect	Difference of direct and	Lower limit of	Upper limit of	P value
	of studies	analysis	comparison	comparison	indirect comparison	95% CI	95% CI	
100mg QM: 200mg Q2W	1	-0.819764033	-0.817285208	-0.84261284	0.025327632	-2.417592314	2.468247577	0.983787738
100mg QM: 300mg Q2M	0	-0.416674676	-	-0.416674676	-	-	-	-
100mg QM: 300mg Q2W	1	-0.867625211	-0.880501624	-0.791828691	-0.088672933	-2.058126265	1.880780399	0.929681409
100mg QM: 300mg QM	1	-0.714066916	-0.559615788	-1.436281383	0.876665595	-1.023876507	2.777207698	0.365955524
100mg QM: 300mg QW	1	-0.866224789	-0.99633344	0.12282381	-1.11915725	-3.280412217	1.042097717	0.310142417
100mg QM: Placebo	1	0.410625443	2.015928136	0.193567405	1.822360731	-0.36107779	4.005799251	0.101872567
200mg Q2W: 300mg Q2M	0	0.403089356	-	0.403089356	-	-	-	-
200mg Q2W: 300mg Q2W	1	-0.047861178	-0.063216416	-0.033758354	-0.029458062	-0.794583091	0.735666967	0.9398483
200mg Q2W: 300mg QM	2	0.105697117	0.142693803	-0.354635595	0.497329398	-0.857229355	1.851888151	0.471768025
200mg Q2W: 300mg QW	1	-0.046460756	-0.179048231	0.089447043	-0.268495275	-1.028116718	0.491126168	0.488455454
200mg Q2W: Placebo	2	1.230389475	1.605246273	1.096727506	0.508518767	-0.378570549	1.395608082	0.261209113
300mg Q2M: 300mg Q2W	0	-0.450950535	-	-0.450950535	-	-	-	-
300mg Q2M: 300mg QM	1	-0.297392239	-0.299242895	-0.264467092	-0.034775803	-2.090942347	2.021390741	0.973555979
300mg Q2M: 300mg QW	0	-0.449550112	-	-0.449550112	-	-	-	-
300mg Q2M: Placebo	1	0.827300119	0.835321669	0.816859103	0.018462566	-1.073161728	1.11008686	0.973555979
300mg Q2W: 300mg QM	1	0.153558295	0.320885836	0.058275337	0.262610499	-0.486386118	1.011607116	0.491959527
300mg Q2W: 300mg QW	5	0.001400422	-0.002988737	0.663344456	-0.666333192	-2.241990851	0.909324466	0.40718742
300mg Q2W: Placebo	5	1.278250654	1.261731013	1.407295805	-0.145564792	-0.787862682	0.496733098	0.656905841
300mg QM: 300mg QW	1	-0.152157873	-0.436717652	0.021104831	-0.457822482	-1.194423621	0.278778657	0.223154133
300mg QM: Placebo	4	1.124692358	1.378128644	0.814134341	0.563994303	-0.154198737	1.282187342	0.123767102
300mg QW: Placebo	5	1.276850231	1.248592518	1.600715904	-0.352123386	-1.074017637	0.369770865	0.339059462
"-" means data not applic	able. IGA, Ir	nvestigator's Glob	oal Assessment.					

Table S4. Assessment of inconsistency in all studies. Outcome: Peak pruritus NRS score, improvement ≥ 3 points

Comparison	Number	Network meta-	Direct	Indirect	Difference of direct and	Lower limit of	Upper limit of	P value
	of studies	analysis	comparison	comparison	indirect comparison	95% CI	95% CI	
100mg QM: 200mg Q2W	1	-0.673829867	-0.589606502	-1.141437937	0.551831435	-1.099370164	2.203033035	0.512455007
100mg QM: 300mg Q2M	0	-0.417488618	-	-0.417488618	-	-	-	-
100mg QM: 300mg Q2W	1	-0.778128855	-0.708651367	-1.086169618	0.377518251	-1.082336322	1.837372825	0.612262529
100mg QM: 300mg QM	1	-0.619908768	-0.613104473	-0.654112806	0.041008333	-1.522190081	1.604206746	0.958993298
100mg QM: 300mg QW	1	-0.818757213	-0.992663711	0.528227844	-1.520891555	-3.286605518	0.244822408	0.091371283
100mg QM: Placebo	1	0.284391023	0.891998039	-0.008209358	0.900207397	-0.322941087	2.123355881	0.149165431
200mg Q2W: 300mg Q2M	0	0.256341249	-	0.256341249	-	-	-	-
200mg Q2W: 300mg Q2W	1	-0.104298988	-0.119044865	-0.093616837	-0.025428029	-0.704548584	0.653692527	0.941498865
200mg Q2W: 300mg QM	2	0.053921098	0.07943396	-0.26869167	0.34812563	-0.800559108	1.496810369	0.552515046
200mg Q2W: 300mg QW	1	-0.144927346	-0.403057209	0.082913933	-0.485971142	-1.146490013	0.174547729	0.149294804
200mg Q2W: Placebo	2	0.95822089	1.130886647	0.803069046	0.327817601	-0.321069253	0.976704455	0.322089229
300mg Q2M: 300mg Q2W	0	-0.360640237	-	-0.360640237	-	-	-	-
300mg Q2M: 300mg QM	1	-0.202420151	-0.170058463	-0.486588254	0.316529792	-1.169238286	1.802297869	0.67627393
300mg Q2M: 300mg QW	0	-0.401268595	-	-0.401268595	-	-	-	-
300mg Q2M: Placebo	1	0.701879641	0.624154309	0.838862	-0.21470769	-1.222530148	0.793114767	0.67627393
300mg Q2W: 300mg QM	1	0.158220086	0.095546894	0.192468221	-0.096921327	-0.727079181	0.533236526	0.763069889
300mg Q2W: 300mg QW	4	-0.040628358	-0.042258813	1.769317255	-1.811576068	-7.463919265	3.840767129	0.529893575
300mg Q2W: Placebo	4	1.062519877	1.069573744	1.010657615	0.058916129	-0.58190355	0.699735809	0.856998272
300mg QM: 300mg QW	1	-0.198848445	-0.379559238	-0.081030039	-0.298529199	-0.902838532	0.305780134	0.332932777
300mg QM: Placebo	4	0.904299791	1.033464588	0.602604029	0.430860559	-0.177050874	1.038771992	0.164791638
300mg QW: Placebo	4	1.103148236	1.075867228	1.292967556	-0.217100328	-0.827444506	0.39324385	0.485701359
"-" means data not applic	able. NRS, N	Numeric Rating S	cale.					

Comparison	Number	Network meta-	Direct	Indirect	Difference of direct and	Lower limit of	Upper limit of	P value
	of	analysis	comparison	comparison	indirect comparison	95% CI	95% CI	
	studies							
100mg QM: 200mg Q2W	1	0.092666619	0.078137111	0.170293751	-0.092156639	-0.555968273	0.371654995	0.696955645
100mg QM: 300mg Q2M	0	0.024159007	-	0.024159007	-	-	-	-
100mg QM: 300mg Q2W	1	-0.043333841	0.042764722	-0.180398337	0.223163059	-0.056558441	0.502884559	0.117895557
100mg QM: 300mg QM	1	-0.001066038	-0.055059777	0.310568725	-0.365628502	-0.75924002	0.027983016	0.068663986
100mg QM: 300mg QW	1	-0.010796117	-0.031252544	0.043151644	-0.074404188	-0.375260877	0.226452502	0.627879049
100mg QM: Placebo	1	-0.032038847	0.01495821	-0.107423704	0.122381914	-0.1514884	0.396252228	0.38112185
200mg Q2W: 300mg Q2M	0	-0.068507612	-	-0.068507612	-	-	-	-
200mg Q2W: 300mg Q2W	1	-0.13600046	-0.03537239	-0.239554711	0.204182322	-0.071079567	0.47944421	0.145987394
200mg Q2W: 300mg QM	2	-0.093732657	-0.113394255	0.088935382	-0.202329636	-0.673053598	0.268394325	0.399539207
200mg Q2W: 300mg QW	1	-0.103462737	-0.109389655	-0.095411115	-0.013978539	-0.288871154	0.260914075	0.920609533
200mg Q2W: Placebo	2	-0.124705467	-0.115229177	-0.157175919	0.041946742	-0.276322621	0.360216106	0.796162954
300mg Q2M: 300mg Q2W	0	-0.067492848	-	-0.067492848	-	-	-	-
300mg Q2M: 300mg QM	1	-0.025225045	0.019342963	-0.177959488	0.197302451	-0.173821044	0.568425946	0.297417905
300mg Q2M: 300mg QW	0	-0.034955124	-	-0.034955124	-	-	-	-
300mg Q2M: Placebo	1	-0.056197854	-0.085655445	0.161235365	-0.24689081	-0.7112894	0.217507781	0.297417905
300mg Q2W: 300mg QM	1	0.042267803	-0.097824499	0.110101685	-0.207926184	-0.405515036	-0.010337331	0.039159761
300mg Q2W: 300mg QW	5	0.032537724	0.031441018	0.130805195	-0.099364177	-0.617612054	0.418883701	0.707076125
300mg Q2W: Placebo	5	0.011294993	0.021817076	-0.241252641	0.263069717	-0.008041403	0.534180837	0.057193427
300mg QM: 300mg QW	1	-0.009730079	0.023807234	-0.03082889	0.054636123	-0.130340035	0.239612282	0.562648858
300mg QM: Placebo	4	-0.030972809	-0.047142415	0.042661082	-0.089803498	-0.307054818	0.127447822	0.417839517
300mg QW: Placebo	5	-0.02124273	-0.0120094	-0.29994504	0.28793564	0.010442364	0.565428916	0.041979886
"-" means data not applicat	ble. AEs, ad	dverse events.						

Table S5. Assessment of inconsistency in all studies. Outcome: ≥1 AEs

Table S6. Assessment of inconsistency in all studies. Outcome: ≥1 SAEs

Comparison	Number	Network meta-	Direct	Indirect	Difference of direct and	Lower limit of	Upper limit of	P value
	of studies	analysis	comparison	comparison	indirect comparison	95% CI	95% CI	
100mg QM: 200mg Q2W	1	1.586263518	1.545924507	1.71121615	-0.165291643	-4.453477422	4.122894136	0.939778373
100mg QM: 300mg Q2M	0	0.420053426	-	0.420053426	-	-	-	-
100mg QM: 300mg Q2W	1	0.909098858	0.900786545	0.917699519	-0.016912974	-2.30360189	2.269775942	0.98843393
100mg QM: 300mg QM	1	0.448790183	0.510825624	0.182763022	0.328062601	-2.867168313	3.523293515	0.84051517
100mg QM: 300mg QW	1	0.997706094 1.578185369 0.		0.751407073	0.826778296	-1.701987797	3.35554439	0.521646884
100mg QM: Placebo	1	0.329410971	0.159630146	0.792897561	-0.633267416	-3.081207301	1.81467247	0.612133091
200mg Q2W: 300mg Q2M	0	-1.166210092	-	-1.166210092	-	-	-	-
200mg Q2W: 300mg Q2W	1	-0.677164661	-0.645137961	-0.715503784	0.070365823	-3.449557364	3.59028901	0.968745998
200mg Q2W: 300mg QM	2	-1.137473335	-0.7752518	-4.314603855	3.539352055	-2.525705665	9.604409776	0.252720985
200mg Q2W: 300mg QW	1	-0.588557424	0.032260862	-1.01734473	1.049605592	-2.525279221	4.624490406	0.564982894
200mg Q2W: Placebo	2	-1.256852547	-1.456421173	1.84352875	-3.299949924	-10.4454183	3.845518452	0.365381308
300mg Q2M: 300mg Q2W	0	0.489045432	-	0.489045432	-	-	-	-
300mg Q2M: 300mg QM	1	0.028736757	-0.252590753	4.075645298	-4.328236051	-10.08086023	1.424388127	0.140302946
300mg Q2M: 300mg QW	0	0.577652668	-	0.577652668	-	-	-	-
300mg Q2M: Placebo	1	-0.090642455	1.074514737	-1.369020612	2.443535349	-0.804148087	5.691218785	0.140302946
300mg Q2W: 300mg QM	1	-0.460308675	-0.389960922	-0.504912143	0.114951221	-2.12921275	2.359115193	0.920031655
300mg Q2W: 300mg QW	5	0.088607236	0.135242574	-0.370971815	0.506214389	-1.661716367	2.674145144	0.647201111
300mg Q2W: Placebo	5	-0.579687886	-0.601078707	0.551169376	-1.152248083	-5.092273797	2.787777631	0.56651925
300mg QM: 300mg QW	1	0.548915911	1.067359745	0.383879859	0.683479886	-1.884420785	3.251380557	0.601900328
300mg QM: Placebo	4	-0.119379212	-0.186980418	0.531485382	-0.7184658	-4.168852557	2.731920956	0.683186588
300mg QW: Placebo	5	-0.668295123	-0.686616181	0.36053544	-1.047151622	-4.910944573	2.81664133	0.595292271
"-" means data not applic	able. SAEs,	serious adverse	events.					

Comparison		f Direct Evidence	Random effects model	RR	95%-C	· (b)	Comparison	Number of Studies	f Di Evio
100mg QM:200m Direct estimate Indirect estimate Network estimate	1	0.83	+	0.72 0.54 0.68	[0.49; 1.04 [0.24; 1.24 [0.49; 0.96]	100mg QM:200mg Direct estimate Indirect estimate Network estimate	g Q2W 1	0
100mg QM:300n Direct estimate Indirect estimate Network estimate	1	0.86	*	0.57 0.44 0.55	[0.41; 0.80 [0.19; 1.04 [0.40; 0.76]	100mg QM:300mg Direct estimate Indirect estimate Network estimate	g Q2W 1	C
100mg QM:300m Direct estimate Indirect estimate Network estimate	1	0.87	+	0.63 0.82 0.65	[0.44; 0.90 [0.34; 2.02 [0.47; 0.91	j	100mg QM:300mg Direct estimate Indirect estimate Network estimate	g QM 1	(
100mg QM:300m Direct estimate Indirect estimate Network estimate	1	0.89	+	0.54 0.87 0.57	[0.39; 0.76 [0.34; 2.22 [0.42; 0.78	i .	100mg QM:300mg Direct estimate Indirect estimate Network estimate	g QW 1	(
100mg QM:Plac Direct estimate Indirect estimate Network estimate	1	0.42	+ + \$	1.51 1.18 1.31	[0.92; 2.50 [0.77; 1.81 [0.95; 1.82	i	100mg QM:Place Direct estimate Indirect estimate Network estimate	bo 1	(
200mg Q2W:300 Direct estimate Indirect estimate Network estimate	1	0.46	*	0.80 0.81 0.81	[0.60; 1.06 [0.62; 1.06 [0.66; 0.98	1	200mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng Q2W 1	(
200mg Q2W:300 Direct estimate Indirect estimate Network estimate	2	0.95		0.95 1.01 0.96	[0.80; 1.14 [0.46; 2.22 [0.81; 1.14	i	200mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng QM 2	
200mg Q2W:300 Direct estimate Indirect estimate Network estimate	1	0.48	*	0.75 0.91 0.83	[0.57; 1.00 [0.70; 1.20 [0.69; 1.01	1	200mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng QW 1	
200mg Q2W:Pla Direct estimate Indirect estimate Network estimate	2	0.49	* * \$	2.03 1.82 1.92	[1.54; 2.67 [1.39; 2.38 [1.58; 2.33	1	200mg Q2W:Plac Direct estimate Indirect estimate Network estimate	ebo 2	3
300mg Q2M:300 Direct estimate Indirect estimate Network estimate	1	0.88		0.91 0.42 0.82	[0.67; 1.23 [0.18; 0.95 [0.62; 1.10	1	300mg Q2M:300n Direct estimate Indirect estimate Network estimate	ng QM 1	
300mg Q2M:Pla Direct estimate Indirect estimate Network estimate	1	0.68	+++	1.38 2.44 1.65	[0.95; 1.99 [1.43; 4.16 [1.22; 2.24	j .	300mg Q2M:Place Direct estimate Indirect estimate Network estimate	ebo 1	
300mg Q2W:300 Direct estimate Indirect estimate Network estimate	1	0.43	*	1.10 1.25 1.19	[1.00; 1.57	i	300mg Q2W:300n Direct estimate Indirect estimate Network estimate	ng QM 1	
300mg Q2W:300 Direct estimate Indirect estimate Network estimate	5	1.00	•	- 7.83	[0.94; 1.14 [0.43; 141.52 [0.94; 1.14	1	300mg Q2W:300n Direct estimate Indirect estimate Network estimate	ng QW 5	
300mg Q2W:Pla Direct estimate Indirect estimate Network estimate	5	0.88	•	2.40 2.27 2.38	[2.10; 2.73 [1.59; 3.23 [2.10; 2.69	1	300mg Q2W:Plac Direct estimate Indirect estimate Network estimate	ebo 5	
300mg QM:300m Direct estimate Indirect estimate Network estimate	1	0.45	+ +	0.86 0.89 0.87	[0.67; 1.11 [0.70; 1.11 [0.74; 1.03	1	300mg QM:300mg Direct estimate Indirect estimate Network estimate	g QW 1	
300mg QM:Plac Direct estimate Indirect estimate Network estimate	4	0.66	*	2.06 1.90 2.01	[1.68; 2.53 [1.43; 2.53 [1.70; 2.37	i	300mg QM:Place Direct estimate Indirect estimate Network estimate	bo 4	
300mg QW:Plac Direct estimate Indirect estimate Network estimate	5	0.88		2.30 2.32 2.30	[2.02; 2.62 [1.63; 3.30 [2.03; 2.60	ĵ	300mg QW:Place Direct estimate Indirect estimate Network estimate	bo 5	

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Comparison	Number of Studies	Direct Evidence	Random effects model	RR	95	i%-CI
100mg QM:200m Direct estimate Indirect estimate	g Q2W 1	0.85		0.55	[0.29; [0.07;	1.06]
Network estimate	g Q2W		*	0.51	[0.28;	0.92]
Direct estimate Indirect estimate Network estimate	1	0.82	*	0.49 0.34 0.46	[0.26; [0.09; [0.26;	0.92] 1.26] 0.81]
100mg QM:300m Direct estimate Indirect estimate Network estimate	g QM 1	0.83	+	0.54 0.52 0.54	[0.29; [0.12; [0.30;	1.02] 2.17] 0.96]
100mg QM:300m Direct estimate Indirect estimate Network estimate	g QW 1	0.89	+	0.37 1.70 0.44	[0.20; [0.32; [0.25;	0.67] 8.93] 0.77]
100mg QM:Place			Ť.			
Direct estimate Indirect estimate Network estimate	1	0.33	+	2.44 0.99 1.33	[0.89; [0.49; [0.75;	6.67] 1.99] 2.36]
200mg Q2W:300r Direct estimate Indirect estimate Network estimate	ng Q2W 1	0.42	+	0.89 0.91 0.90	[0.53; [0.59; [0.64;	1.49] 1.41] 1.26]
200mg Q2W:300r Direct estimate Indirect estimate Network estimate	ng QM 2	0.93		1.08 0.76 1.06	[0.79; [0.25; [0.78;	1.48] 2.31] 1.42]
200mg Q2W:300r Direct estimate Indirect estimate Network estimate	ng QW 1	0.47	+	0.67 1.09 0.87	[0.41; [0.69; [0.62;	1.08] 1.71] 1.20]
200mg Q2W:Plac Direct estimate Indirect estimate Network estimate	ebo 2	0.47	+ + \$	3.10 2.23 2.61	[1.93; [1.43; [1.89;	4.96] 3.49] 3.60]
300mg Q2M:300n Direct estimate Indirect estimate Network estimate	ng QM 1	0.90	+	0.84 0.61 0.82	[0.52; [0.15; [0.52;	1.36] 2.51] 1.28]
300mg Q2M:Plac Direct estimate Indirect estimate Network estimate	ebo 1	0.64	+ + +	1.87 2.31 2.02	[1.02; [1.03; [1.24;	3.42] 5.18] 3.27]
300mg Q2W:300r Direct estimate Indirect estimate Network estimate	ng QM 1	0.35	+	1.10 1.21 1.17	[0.66; [0.83; [0.87;	1.83] 1.76] 1.58]
300mg Q2W:300r Direct estimate Indirect estimate Network estimate	ng QW 4	1.00		0.96 	[0.81; [0.02; 16 [0.81;	1.14] 67.56] 1.14]
300mg Q2W:Plac Direct estimate Indirect estimate Network estimate	ebo 4	0.88	-	2.91 2.75 2.89	[2.33; [1.51; [2.35;	3.64] 5.01] 3.56]
300mg QM:300mg Direct estimate Indirect estimate Network estimate	g QW 1	0.39	+	0.68	[0.43; [0.63; [0.61:	1.09] 1.35] 1.10]
300mg QM:Place Direct estimate Indirect estimate	bo 4	0.70	*	2.81 1.83 2.47	[2.01; [1.10;	3.92] 3.04]
Network estimate 300mg QW:Place Direct estimate Indirect estimate	bo 4	0.87	*	2.47 2.93 3.64	[1.87; [2.36; [2.06;	3.26] 3.64] 6.45]
Network estimate			0.001 0.1 1 10 10	3.01 7	[2.46;	3.69]

(c)

Random effects model

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0.1 0.5 1 2 10 RR

95%-CI

0.44 [0.21; 0.95] 0.43 [0.04; 4.38] 0.44 [0.21; 0.91]

0.41 [0.20; 0.88] 0.45 [0.07; 2.80] 0.42 [0.21; 0.84]

0.57 [0.26; 1.27] 0.24 [0.04; 1.33] 0.49 [0.24; 1.01]

0.37 [0.18; 0.77] 1.13 [0.15; 8.62]

0.42 [0.21; 0.84]

- 7.51 [0.97; 58.28] 1.21 [0.57; 2.58] 1.51 [0.74; 3.06]

0.94 [0.54; 1.63] 0.97 [0.57; 1.64] 0.95 [0.65; 1.40]

1.15[0.80;1.67]0.70[0.19;2.58]1.11[0.78;1.59]

0.84 [0.49; 1.43] 1.09 [0.64; 1.88] 0.95 [0.65; 1.40]

4.98[2.32; 10.66]2.99[1.90; 4.72]3.42[2.32; 5.06]

0.74 [0.46; 1.19] 0.77 [0.10; 5.68] 0.74 [0.47; 1.18]

2.31 [1.12; 4.73] 2.26 [1.00; 5.14]

2.29 [1.33; 3.93]

1.38[0.76;2.51]1.06[0.68;1.66]1.17[0.81;1.67]

1.00[0.88;1.13]1.94[0.40;9.34]1.00[0.88;1.14]

3.53[2.84; 4.38]4.08[2.23; 7.48]3.59[2.93; 4.40]

0.65 [0.36; 1.15] 1.02 [0.65; 1.61]

0.86 [0.60; 1.23]

3.97[2.45; 6.42]2.26[1.32; 3.85]3.08[2.15; 4.40]

3.49 [2.84; 4.28]

4.96 [2.48; 9.90] 3.59 [2.95; 4.36]

Fig. S1. Forest plots of pairwise meta-analyses and network meta-analyses of efficacy.

Outcomes: (a) EASI-50; (b) IGA score 0 or 1 (c) Peak pruritus NRS score, improvement ≥ 3 points

(a)	Comparison	Number of Studies	Direct Evidence	Random effects model	RR	95%-CI	(b) •		lumber of Studies	Direct Evidence	Random effects model	RR		95%-CI
	100mg QM:200mg Direct estimate Indirect estimate Network estimate	1 Q2W 1	0.84		1.19	0.90; 1.30] 0.77; 1.81] 0.93; 1.30]	D	00mg QM:200mg irrect estimate indirect estimate letwork estimate	Q2W 1	0.76		4.69 5.54 4.89	[0.13;	39.03] 230.35] 30.82]
	100mg QM:300mg Direct estimate Indirect estimate Network estimate	1 Q2W 1	0.61	+++++++++++++++++++++++++++++++++++++++	0.83	0.88; 1.24] 0.67; 1.04] 0.84; 1.10]	D	00mg QM:300mg irrect estimate indirect estimate letwork estimate	Q2W 1	0.51	++	2.46 2.50 2.48	[0.50; [0.49; [0.79;	12.79]
	100mg QM:300mg Direct estimate Indirect estimate Network estimate	1 QM	0.85	_+_ 	- 1.36 [0.81; 1.10] 0.95; 1.96] 0.87; 1.15]	D	00mg QM:300mg irrect estimate adirect estimate letwork estimate	QM 1	0.81	+	1.67 1.20 1.57	[0.42; [0.07; [0.45;	21.33]
	100mg QM:300mg Direct estimate Indirect estimate Network estimate	1 QW 1	0.73		1.04 [0.83; 1.13] 0.81; 1.35] 0.86; 1.13]	D	00mg QM:300mg irrect estimate adirect estimate letwork estimate	QW 1	0.30	+	4.85 2.12 2.71	[0.58; [0.53; [0.85;	
	100mg QM:Placek Direct estimate Indirect estimate Network estimate	1	0.62		0.90	0.86; 1.20] 0.72; 1.11] 0.85; 1.11]	D	00mg QM:Placebo irrect estimate adirect estimate letwork estimate	1	0.73	+	1.17 2.21 1.39	[0.33; [0.27; [0.47;	17.94]
	200mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng Q2W 1	0.51	↓ ↓ ↓	0.79 [0.80; 1.17] 0.65; 0.96] 0.76; 1.00]	D	00mg Q2W:300mg irrect estimate adirect estimate letwork estimate	g Q2W 1	0.54	+++	0.52 0.49 0.51	[0.05; [0.04; [0.09;	6.57]
	200mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng QM 2	0.90	 	1.09	0.77; 1.03] 0.70; 1.71] 0.79; 1.05]	D	00mg Q2W:300mg irrect estimate adirect estimate letwork estimate	g QM 2	0.90		0.46 0.01 0.32	[0.07; [0.00; [0.05;	3.21] 4.19] 2.02]
	200mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng QW 1	0.58	+++	0.91 [0.75; 1.07] 0.74; 1.12] 0.79; 1.03]	D	00mg Q2W:300mg irrect estimate indirect estimate letwork estimate	g QW 1	0.41		1.03 0.36 0.56	[0.07; [0.04; [0.10;	
	200mg Q2W:Place Direct estimate Indirect estimate Network estimate	2	0.77		0.85 [0.77; 1.04] 0.65; 1.13] 0.77; 1.01]	D	00mg Q2W:Placel irect estimate indirect estimate letwork estimate	2	0.94		0.23 6.32 0.28	[0.04; [0.01; 6 [0.05;	435.35]
	300mg Q2M:300m Direct estimate Indirect estimate Network estimate	IG QM 1	0.77		0.84 [0.85; 1.22] 0.60; 1.16] 0.83; 1.14]	D In N	00mg Q2M:300mg birect estimate bdirect estimate letwork estimate	1	0.94	÷	0.78 58.89 1.03	[0.23; 15	3.37] 3339.30] 4.25]
	300mg Q2M:Place Direct estimate Indirect estimate Network estimate	ebo 1	0.88	-+- &	1.17	0.78; 1.08] 0.76; 1.82] 0.81; 1.10]	D	00mg Q2M:Placet birect estimate birect estimate letwork estimate	1	0.52		2.93 0.25 0.91	[0.31; [0.02; [0.18;	
	300mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng QM 1	0.33	-+- ¢	1.12 [0.77; 1.07] 1.00; 1.25] 0.95; 1.14]	D In N	00mg Q2W:300mg irect estimate indirect estimate etwork estimate	1	0.39	++	0.68 0.60 0.63	[0.12; [0.15; [0.21;	2.44]
	300mg Q2W:300m Direct estimate Indirect estimate Network estimate	ng QW 5	0.99	*	1.14	0.98; 1.09] 0.68; 1.91] 0.98; 1.09]	D In N	00mg Q2W:300mg priect estimate ndirect estimate letwork estimate	5	0.91	*	1.14 0.69 1.09	[0.59; [0.09; [0.58;	5.44]
	300mg Q2W:Place Direct estimate Indirect estimate Network estimate	5	0.96	*	0.79 [0.97; 1.08] 0.60; 1.02] 0.96; 1.07]	D In N	00mg Q2W:Placel priect estimate ndirect estimate letwork estimate	5	0.98		0.55 1.74 0.56	[0.32; [0.04; [0.33;	86.01]
	300mg QM:300mg Direct estimate Indirect estimate Network estimate	1 QW	0.39	++	0.97 [0.89; 1.18] 0.86; 1.09] 0.91; 1.08]	D In N	00mg QM:300mg virect estimate direct estimate letwork estimate	1	0.24	++	2.91 1.47 1.73	[0.31; [0.42; [0.58;	27.22] 5.18] 5.20]
	300mg QM:Placet Direct estimate Indirect estimate Network estimate	4	0.82	*	1.04 [0.87; 1.05] 0.86; 1.27] 0.89; 1.05]	D In N	00mg QM:Placebo virect estimate direct estimate letwork estimate	4	0.91	+	0.83 1.70 0.89	[0.29; [0.06; [0.32;	45.40]
	300mg QW:Placel Direct estimate Indirect estimate Network estimate	5	0.97	0.75 1 1.5	0.74	0.94; 1.04] 0.56; 0.97] 0.93; 1.03]	D	00mg QW:Placebo birect estimate birect estimate letwork estimate	5	0.98	0.001 0.1 1 10 1000	0.50 1.43 0.51	[0.30; [0.03; [0.31;	66.05]

Fig. S2. Forest plots of pairwise meta-analyses and network meta-analyses of safety.

Outcomes: (a) ≥1 AEs; (b) ≥1 SAEs