SUPPLEMENTARY MATERIAL

Comparative Efficacy of Targeted Systemic Therapies for Moderate to Severe Atopic Dermatitis without Topical Corticosteroids: Systematic Review and Network Meta-analysis

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Systematic literature review

The process of study identification was divided into 1) searches of bibliographic databases to identify published studies and 2) non-database search methods to identify in-process, unpublished, or grey literature [1]. The searches were conducted following guidance from NICE and the Canadian Agency for Drugs and Technologies in Health (CADTH) Grey Matters report for searching health-related grey literature [2,3]

Bibliographic databases were searched from database inception using predefined search strategies. The search strategy for the clinical systematic literature review was designed as follows:

Search strategy
1 Dermatitis, Atopic/ 2 exp Eczema/ 3 (atopic* adj3 (Dermatiti* or neurodermatitis)).ti,ab,kw,kf,ot. 4 Coca Sulzberger.ti,ab,kw,kf,ot. 5 Eczema*.ti,ab,kw,kf,ot. 6 1 or 2 or 3 or 4 or 5
7 Janus Kinase Inhibitors/ 8 (Upadacitinib* or Rinvoq* or ABT 494 or ABT-494 or ABT494 or 4RA0KN46E0 or 1310726-60-3 or 1607431-21-9).ti,ab,kf,kw,ot,rn,nm. 9 (Dupilumab* or dupixent* or regn 668 or REGN-668 or regn668 or sar 231893 or sar-231893 or sar231893 or 420K487FSG or 1190264-60-8).ti,ab,kf,kw,ot,rn,nm. 10 exp phototherapy/ 11 (Phototherap* or light therap* or ultraviolet or ultra violet or ultra-violet or broadband or broad band or narrowband or narrow band or UVB or PUVA or Psoralen or UVA or UVA1).ti,ab,kf,kw,ot,rn,nm. 12 Azathioprine/ 13 (Azathioprin* or arathioprin* or AZA or aza-q or azafalk* or azahexal* or azamedac* or azamun* or azanin* or azapin* or azapress* or azaprin* or azarex* or azasan* or azathiodura* or azathioprim* or azathioprinum* or azathiopurin* or azathropsin* or azatioprin* or azatox* or azatrilem* or azopi* or azoran* or azothioprin* or colinsan* or immuran* or immurel* or immuthera* or imunen* or imuprin* or imuran* or imurek* or imurel* or imuren* or muran* or rorasul* or thioazeprin* or thiazepin* or thioprin* or transimun* or zytrim* or AI3-50290 or bw 57 322 or bw-57322 or bw57322 or bw57-322 or bw57322 or CCRIS 62 or CCRIS-62 or CCRIS62 or ccucol* or "EINECS 207-175-4" or HSDB 7084 or HSDB-7084 or HSDB7084 or NCI-C03474 or nsc 39084 or nsc-39084 or nsc39084 or MRK240IY2L or 446-86-6).ti,ab,kf,kw,ot,rn,nm. 14 Ciclosporin/ 15 (Ciclosporin* or abrammun* or aqua-stasis* or aquastasis* or arpimun* or cequa* or ciclomulsion* or cicloral* or ciclosporina* or ciclosporine* or ciclosporinum* or cipol* or consupren* or cyclasol* or cyclo-derm* or cyclokat* or cyclosporin* or deximune* or equoral* or gengraf* or hydro-stasis* or ikervis* or iminoral* or implanta* or imusporin* or neoplanta* or neoral-sandimmun* or neoral* or neural* or neuro-stat* or neurostat* or opsisporin* or optimmun* or padciclo* or papilock* or pulminiq* or "Ramihyphin A" or restasis* or restaysis* or sanciclo* or sandimmun* or sandimun* or sangcya* or vekacia* or verkazia* or "27400" or "de 076" or "DRG 0275" or "nm 0133" or "opph 088" or "sti 0529" or 27 400 or 27-400 or 59865-13-3 or "adi 628" or "adi-628" or "adi628" or CCRIS 1590 or CCRIS-1590 or CCRIS1590 or cgc 1072

or cgc-1072 or cgc1072 or de-076 or de076 or Debio088 or DRG-0275 or DRG0275 or HSDB 6881 or HSDB-6881 or HSDB6881 or lx
201 or lx-201 or lx201 or mc203 or "mc 203" or "mtd 202" or mtd-202 or mtd202 or nm 133 or nm-0133 or nm-133 or nm133 or
nm0133 or nova 22007 or nova-22007 or nova22007 or NSC 290193 or NSC-290193 or NSC290193 or ol 27400 or ol-27-400 or
ol-27400 or ol27400 or olo 400 or olo 500 or olo-400 or olo-500 or olo400 or olo500 or opph-088 or opph088 or otx 101 or
otx-101 or otx101 or p 3072 or p-3072 or p3072 or S 7481F1 or S-7481F1 or S7481F1 or sang 35 or sang-35 or sang35 or
SDZ-OXL-400 or sp 14019 or sp-14019 or sp14019 or sti-0529 or sti0529 or t1580 or t-1580 or t1580 or 83HN0GTJ6D or
63798-73-2 or 79217-600 or 59865-13-3).ti,ab,kf,kw,ot,rn,nm.
16 Methotrexate/
17 (Methotrexat* or abitrexat* or alltrex* or amethopterin* or ametopterin* or antifolan* or artrait* or atrexel* or
bendatrexat* or biotrexat* or brimexat* or canceren* or carditrex* or dermotrex* or ebetrex* or emtexat* or emthexat* or
emtrexat* or enthexat* or farmitrexat* or farmotrex* or fauldexato* or folex* or glutamic acid or hdmtx or ifamet* or
imeth* or intradose* or jylamvo* or lantarel* or ledertrexat* or lumexon* or maxtrex* or medsatrexat* or meisusheng* or
metatrexan* or metex* or methoblastin* or methohexat* or methotrat* or Methotrexat-Ebewe or methotrexat* or methotrexat*
or methotrexatum* or methoxtrexat* or methylaminopterin* or methylfolic acid or methylpteroylglutamic acid or metical*
or metoject* or metothrexat* or metotrexat* or metotrexato* or metotrexin* or metrex* or mexate-aq or mexat* or MTX or
neotrexat* or nordimet* or novatrex* or otrexup* or rasuvo* or reumatrex* or rheumatrex* or texat* or texorat* or
trexall* or trexan* or xaken* or xatmep* or zexat* or "EINECS 200-413-8" or 3IG1E710ZN or AI325299 or AI3-25299 or CCRIS
1109 or cl 14377 or cl-14377 or cl14377 or EMT 25299 or EMT-25299 or EMT25299 or HSDB 3123 or HSDB-3123 or HSDB3123 or
mpi 5004 or mpi-5004 or mpi5004 or nsc 740 or nsc-740 or nsc740 or R 9985 or R-9985 or R9985 or YL5FZ2Y5U1 or 15475-56-6
or 59-05-2 or 7413-34-5).ti,ab,kf,kw,ot,rn,nm.
18 Alitretinoin/
19 (Alitretinoin* or alitretinoinum* or cehado* or hanzema* or panretin* or panretyn* or panrexin* or retinoic acid*
or toctino* or tretinoin* or agn 192013 or agn-192013 or agn192013 or alrt 1057 or alrt-1057 or alrt1057 or bal 4079 or
bal-4079 or bal4079 or CCRIS 7098 or CCRIS-7098 or CCRIS7098 or HSDB 7186 or HSDB-7186 or HSDB7186 or LG100057 or lgd
100057 or lgd 1057 or lgd-100057 or lgd-1057 or lgd100057 or lgd1057 or nsc 659772 or nsc-659772 or nsc659772 or
1UA8E65KDZ or 5300-03-8).ti,ab,kf,kw,ot,rn,nm.
20 Mycophenolate Mofetil/
21 (mycophenolat* mofetil* or MMF or cell cept* or cellcept* or cellmun* or cellsept* or munoloc* or myclausen* or
mycophenolic acid or myfenax* or "168396" or HSDB 7436 or HSDB-7436 or HSDB7436 or rs 61443 or rs-61443 or rs61443 or
9242ECW6R0 or 128794-94-5).ti,ab,kf,kw,ot,rn,nm.
22 (tralokinumab* or cat 354 or cat-354 or cat354 or GK1LYB375A or 1044515-88-9).ti,ab,kf,kw,ot,rn,nm.
23 (baricitinib* or olumiant* or "incb 028050" or incb-028050 or incb028050 or incb 28050 or incb-28050 or incb28050

or ly 3009104 or ly-3009104 or ly3009104 or ISP4442I3Y or 1187594-09-7).ti,ab,kf,kw,ot,rn,nm.
24 (abrocitinib* or "pf 04965842" or pf-04965842 or pf04965842 or pf 4965842 or pf-4965842 or pf4965842 or
73SM5SF3OR or 1622902-68-4).ti,ab,kf,kw,ot,rn,nm.
25 Prednisolone/
26 (Prednisolone or Adelcort* or Ak-Pred* or Antisolon* or Aprednislon* or Benisolon* or Berisolon* or Bubbli-Pred*
or Caberdelt* or Cambison* or Capsoid* or "co hydeltra*" or Codelcorton* or Compresolon* or Cordrol* or Cortadelton* or
Cortalon* or Cortelinter* or Cortisolon* or Cotogesic* or Cotolon* or Dacortin* or Decaprednil* or Decortin* or Decortril* or "dehydro cortex" or "dehydro hydrocortison*" or Dehydrocortex or Dehydrocortisol* or Dehydrohydrocortison*
or Delcortol* or "delta 1 17 hydroxycorticosterone 21 acetate" or "delta 1 hydrocortisone" or (Delta adj Cortelan*) or
delta cortef* or delta cortril* or "delta f" or "delta hycortol*" or "delta hydrocortisone*" or "delta ophticor*" or "delta stab" or delta-hydrocortison* or "delta1 dehydrocortisol*" or "delta1 dehydrohydrocortison*" or "delta1 hydrocortison*" or Deltacortef* or Deltacortenol* or Deltacortenolo* or Deltacortil* or Deltaderm* or Deltaglycortril*
or Deltahycortol* or Deltahydrocortison* or Deltaophticor* or Deltasolon* or Deltason* or Deltastab* or Deltidrosol* or
Deltisilon* or Deltisolon* or Deltolasson* or Deltolasson* or Deltoson* or Depopredat* or Depo predat* or Dermosolon* or
"Derpo PD" or Dhasolon* or "di adreson f" or "Di-adreson F" or "di-adreson-f" or Diadreson* or Dicortol* or Domucorton*
or Donisolon* or Dydeltron* or "Eazolin D" or Encortelon* or Equisolon* or Erbacort* or Erbason* or Estilson* or
Fernisolon* or Glistelon* or Hefasolon* or Hostacortin* or Hydeltra* or Hydeltrasol* or Hydeltron* or Hydrelta* or
Hydrocortancyl* or Hydrocortidelt* or Hydrodeltalon* or Hydrodeltison* or Hydroretrocortin* or Inflamas* or Inflanefran*
or Insolon* or Keteocort* or Key pred* or Klismacort* or Lenisolon* or Lentoson* or Leocortol* or Liquipred* or "liquid
pred" or lygal kopftinktur or mediasolon* or meprisolon* or meprisolon* or metacortalon* or metacortalon* or metacortandralon* or metacortandralon* or metacortelon* or meti derm* or meti-derm* or meticortelon* or metiderm* or
Millipred* or Morlon* or Mydrapred* or neo delta* or nisolon* or opredson* or Orason* or Panafcortelon* or Panafort* or
Paracortol* or Paracotol* or Pediapred* or Phlogex* or Poly-Pred* or PRDL or pre cortisyl* or preconin* or precortalon*
or Precortancyl* or Precortilon* or Precortisyl* or Pred ject* or Predject* or Predacort* or Predalon* or Predartrin* or
Predat* or Predeltilon* or Predisol* or Predisyr* or predne dom* or prednecort* or prednedom* or prednelan* or predni
coelin* or predni h tablinen* or predni-helvacort* or Prednicen* or Prednicoelin* or Prednicort* or Prednicortelon* or
prednifor drops* or Predniliderm* or Predniment* or Predniretard* or Prednis* or Prednisil* or Prednisolone* or prednisolon* or Prednisolonum* or Prednivet* or Prednorsolon* or Prednorsolon* or Predonin* or Predonin* or Predorgasolon* or Predorgasolon* or Preflam* or Prelon* or Prenilon* or Prenin* or Prenolon* or Preventan* or Prezolon*
or Rolison* or Rubycort* or Scherisolon* or Scherisolon* or Serilon* or Solondo* or Solon* or Solupren* or Solupren* or
Spiricort* or Spolotan* or Steran* or Steran* or Sterolon* or Supercortisol* or Supercortizol* or Taracortelon* or
Ulacort* or Ultracort* or Walesolon* or Wysolon* or NSC 9120 or NSC-9120 or NSC9120 or NSC 9900 or NSC-9900 or NSC9900

	or CCRIS 980 or HSDB 3385 or HSDB-3385 or HSDB3385 or K 1557 or K1557 or 9PHQ9Y1OLM or 50-24-8).ti,ab,kf,kw,ot,rn,nm.
27	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28	randomized controlled trial.pt.
29	controlled clinical trial.pt.
30	randomi*.ab.
31	placebo.ab.
32	clinical trials as topic.sh.
33	randomly.ab.
34	(trial or trail).ti.
35	("Phase 3" or "phase3" or "phase III" or P3 or "PIII").ti,ab,kw,kf,ot.
36	Clinical Trial, Phase III/
37	("Phase 2" or "phase2" or "phase II" or P2 or "PII").ti,ab,kw,kf,ot.
38	Clinical Trial, Phase II/
39	(open adj1 label*).ti,ab,kf.
40	28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39
41	"Systematic Review"/
42	(systematic adj3 review$).ti,ab,kf.
43	Meta-Analysis/
44	meta anal$.ti,ab,kf.
45	41 or 42 or 43 or 44
46	40 or 45
47	6 and 27 and 46
48	exp animals/ not humans.sh.
49	47 not 48

The Cochrane Collaboration's Highly Sensitive Search Strategy (HSSS) merged with the Cooper et al. P3 filter was used [4,5].

The following bibliographic databases were searched for the clinical systematic literature review:

- MEDLINE®, 1946 to present (OVID)
- MEDLINE In-Process & Other Non-Indexed Citations (OVID)
- MEDLINE Epub Ahead of Print (OVID)
- Embase, 1980 to present (OVID)
- Latin American & Caribbean Health Sciences Literature (LILACS) database, 1982 to present
- PsycINFO, 1806 to present (OVID)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley)
- Cochrane Database of Systematic Reviews (CDSR) (Wiley)
- PubMed (NLM)—e-publications only [6]
- Database of Abstracts of Reviews of Effects (DARE) (CRD)
- Health Technology Assessment (HTA) database (CRD)
- International Network of Agencies for HTA (INAHTA) database

In addition to bibliographic databases, several non-database sources were also searched [7]:

- Trial registries:
    - ClinicalTrials.gov
    - EU Clinical Trials Register
    - World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP)
- Websites:
    - The National Institute for Health and Care Excellence (NICE)
    - Scottish Medicines Consortium (SMC)
    - Pharmaceutical Benefits Advisory Committee (PBAC)
    - Canadian Agency for Drugs and Technologies in Health (CADTH)

Conference abstracts were identified through searches of:

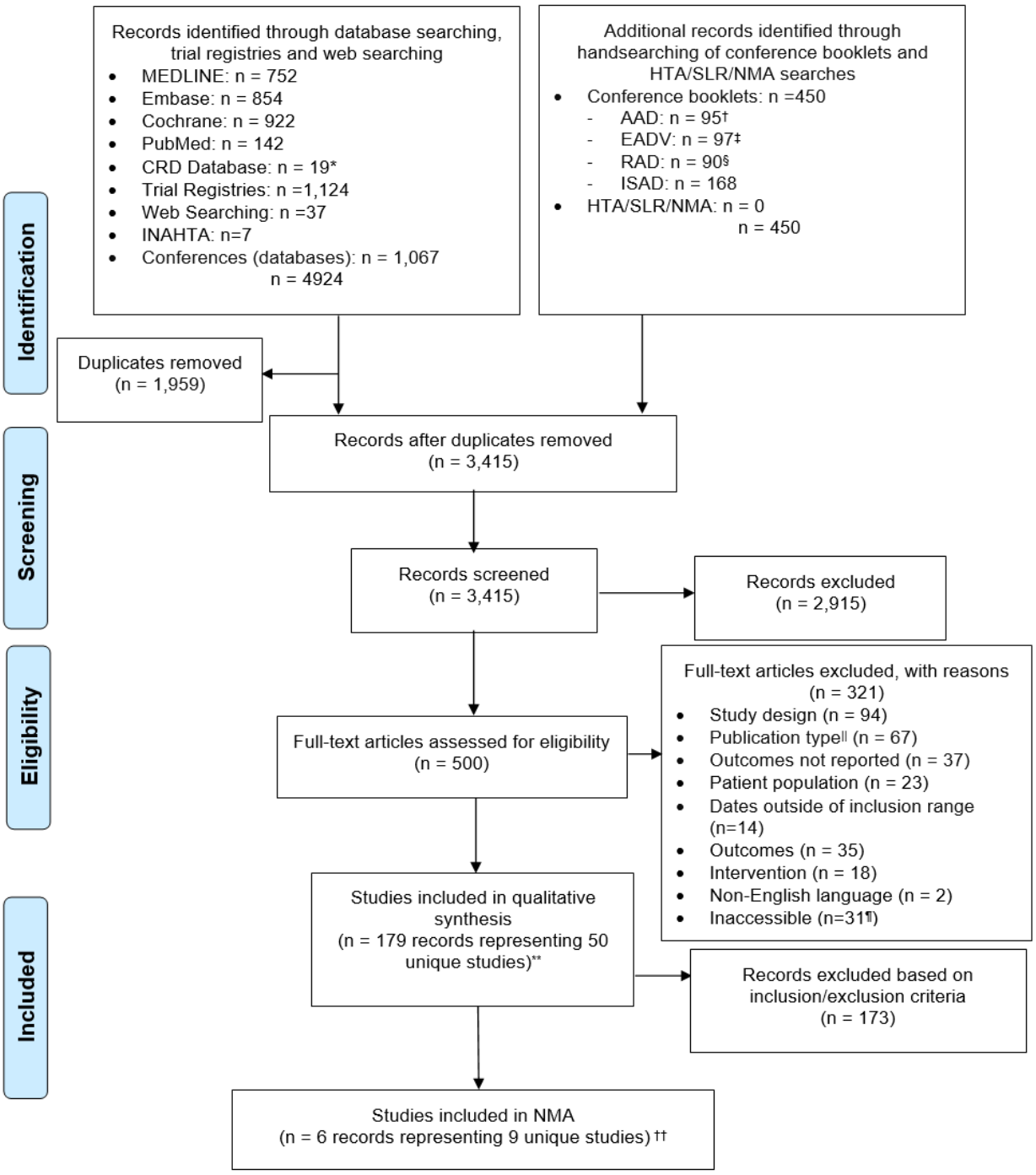
- Embase, 1980 to present (OVID)
- Conference Proceedings Citation Index-Science (CPCI-S), 1990 to present (Web of Science, Clarivate Analytics)

These searches were date limited 2018–2021, in-line with the inclusion criteria for conference data.

In addition, the following conferences were hand-searched for the years 2018–2021 to identify relevant studies:

- American Academy of Dermatology (AAD) hand-searched via the Journal of the American Academy of Dermatology
- European Academy of Dermatology and Venereology (EADV) via the EADV Programs and ePoster lists
- International Symposium on Atopic Dermatitis (ISAD) via the British Journal of Dermatology abstract booklet
- Revolutionizing Atopic Dermatitis (RAD) via the British Journal of Dermatology abstract booklet

Figure S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram



*CRD Databases were not searched for the May 2021 update as they are no longer updated. Instead, the INAHTA Database was searched.
†A total of 56 entries from the AAD conference were screened in the initial search. The remaining 25 entries were identified through database searching and were pooled under Conferences (databases): n = 1,067.
‡After literature searching, 25 conference proceedings from EADV 2018 were unretrievable.
§RAD 2020 (April) was searched. Abstracts from the inaugural 2019 conference were inaccessible.
||Publication types excluded were commentaries, letters to the editor, review papers, consensus reports.

¶After title-abstract screening, 31 conference proceedings from EADV 2020 did not progress in the SLR due to access issues.
**Of the 179 included records, 45 were primary publications, 132 were associated publications, and two were clinical trial registry entries for UPA.
††The discrepancy between the number of records (n=6) and number of unique studies (n=9) is because three of the primary records each published the findings from two included studies.

Systematic literature review study selection

Studies were assessed for relevance using the predefined Population, Intervention, Comparator, Outcome, and Study design (PICOS) criteria outlined in Table S1. Trials that did not include at least one of the interventions of interest in a treatment arm were excluded.

Two levels of screening (title–abstract and full-text screening) using the PICOS criteria were performed during study selection. Title–abstract screening was conducted independently by two researchers using Covidence systematic review software and selecting the option of "yes/no/maybe" for article inclusion. The voting system worked as follows: two votes of "yes" moved the record forward to full-text screening; two votes of "no" moved the record to irrelevant; votes consisting of "yes"/"no" and "maybe" were placed into a conflicts list where reviewers discussed whether to move the reference forward to full-text or to the irrelevant category. This system ensured studies were advanced to full-text screening in case of doubt by either researcher. No study was excluded at title–abstract screening due to insufficient information. Studies reported in languages other than English were tagged.

The full-text publications of citations that progressed through title–abstract screening were retrieved for further review. As with title–abstract screening, screening of full-text publications was conducted by two independent researchers using Covidence systematic review software. The same inclusion and exclusion criteria used in title–abstract screening were applied during full-text screening. Disagreements between researchers were resolved by discussion or by review with a third researcher. Studies were excluded if they did not meet PICOS inclusion criteria or were duplicate publications. Any study excluded during full-text screening was tagged with a reason for exclusion based on the PICOS criteria.

Table S1. PICOS criteria used in the NMA

Criteria	Inclusion criteria	Exclusion criteria
Population	• Adults and adolescents (≥12 years) AND • Patients with moderate to severe AD* with inadequate response to TCS or TCI	• Children (<12 years) • Patients with other active skin diseases or infections requiring systemic treatment, or those that would interfere with assessment of AD lesions
Intervention	Any formulation of the following (without combination corticosteroids; concomitant therapies [e.g., emollients]; rescue therapy and/or retreatment): • Upadacitinib • IL-4 or -13 inhibitors • JAK inhibitors	Studies only containing: • Systemic immunosuppressants • Topical retinoids • Phototherapy • Prednisolone Studies containing: • Use of concomitant TCS or TCI therapies
Comparators	• Placebo • Active intervention (i.e., head-to-head trials)	Studies only containing: • TCS • Systemic immunosuppressants • Topical retinoids • Phototherapy • Prednisolone
Outcomes	Efficacy • EASI • IGA PRO • Pruritus NRS‡	Studies only containing: • SCORAD • BSA • POEM • DLQI or CDLQI for adolescents† • HADS • EQ-5D overall, or any of 5 domains, or EQVAS, or EQ-5D-Y • SF-36 • Safety analyses
Study design	• Randomized controlled trials (phase III, IV) • Randomized crossover/cluster trials, provided randomized phase is at least 12 weeks	• Randomized controlled trials (phases I, II) • Long-term follow-up studies (e.g., open-label [OLE] follow-up studies with continuation of treatment) • Dose-ranging randomized controlled trials (that include a control arm) • Trial registries
Limits / language restriction	• No restrictions on year or region • English language¶ • Conference presentations published in 2018 or later**	• Conference presentations published before 2018**

AD, atopic dermatitis; BSA, body surface area; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EQ-5D, European Quality of Life-5 Dimensions; ED-5D-Y, EQ-5D - youth; EQVAS, EQ-5D visual analogue scale; HADS, Hospital Anxiety and Depression Scale; IGA, Investigator Global Assessment for Atopic

Dermatitis; IL-4, interleukin-4; IL-13, interleukin-13; JAK, Janus kinase; NRS, numerical rating scale; OLE, open-label extension; POEM, Patient-Oriented Eczema Measure; PRO, Patient-Reported Outcome; SCORAD, SCORing Atopic Dermatitis; SF-36, Short Form-36 Health Survey; TCS, topical corticosteroid
*Moderate to severe disease was defined according to thresholds for EASI, IGA, BSA, and pruritus as reported in each study.
†The CDLQI tool is validated for patients 4–16 years of age. The clinical systematic literature review identified studies reporting results for adolescents 12–16 years of age.
‡May include alternative names for outcome, such as peak pruritus NRS, worst pruritus NRS, itch NRS.
¶Languages other than English were tagged during title–abstract screening and did not move forward to full-text screening.
**Conference presentations were limited to those published in 2018 or later as those from prior to 2018 were assumed to have been published outside of a conference presentation since that time.

Data extraction

Data extracted from studies in the clinical systematic literature review included study design, population inclusion and exclusion criteria, baseline population characteristics, intervention(s) and comparators, primary and secondary outcomes, and time factors including length of treatment and duration of follow-up.

One researcher extracted relevant data from the included studies, while a second researcher independently audited the data extraction for accuracy and completeness. Each study had all relevant data extracted from both the primary publication and any relevant abstracts presenting more recent data cuts or subgroup analyses. Discrepancies in the data extracted were discussed and resolved through consensus or by involving a third researcher.

A comprehensive data extraction form (DEF) was created in Microsoft Excel to compile the data. One researcher extracted relevant data from the included studies, while a second researcher independently audited the data extraction for accuracy and completeness.

Randomized controlled trial quality assessment

Studies were critically appraised for methodological quality using validated tools in accordance with NICE requirements as specified in Section 2.5.2 and 3.1 of the *NICE Single technology appraisal: User guide for company evidence submission template (PMG24)*. For randomized clinical trials, the checklist recommended in the NICE *Single technology appraisal: User guide for company evidence submission template* was employed (Table S2) [8].

Included studies were evaluated using a fixed set of domains of bias focused on different aspects of trial design, conduct, and reporting. Seven specific domains were examined: random sequence generation, allocation concealment, blinding of participants, blinding of investigators, blinding of outcome assessors, incomplete outcome data, selective reporting, and other potential sources of bias that may affect internal or external validity and generalizability of the study findings to the general population. Two researchers independently assessed each study and disagreements were resolved by discussion or by a third researcher.

Table S2. Complete quality assessment of each identified clinical study

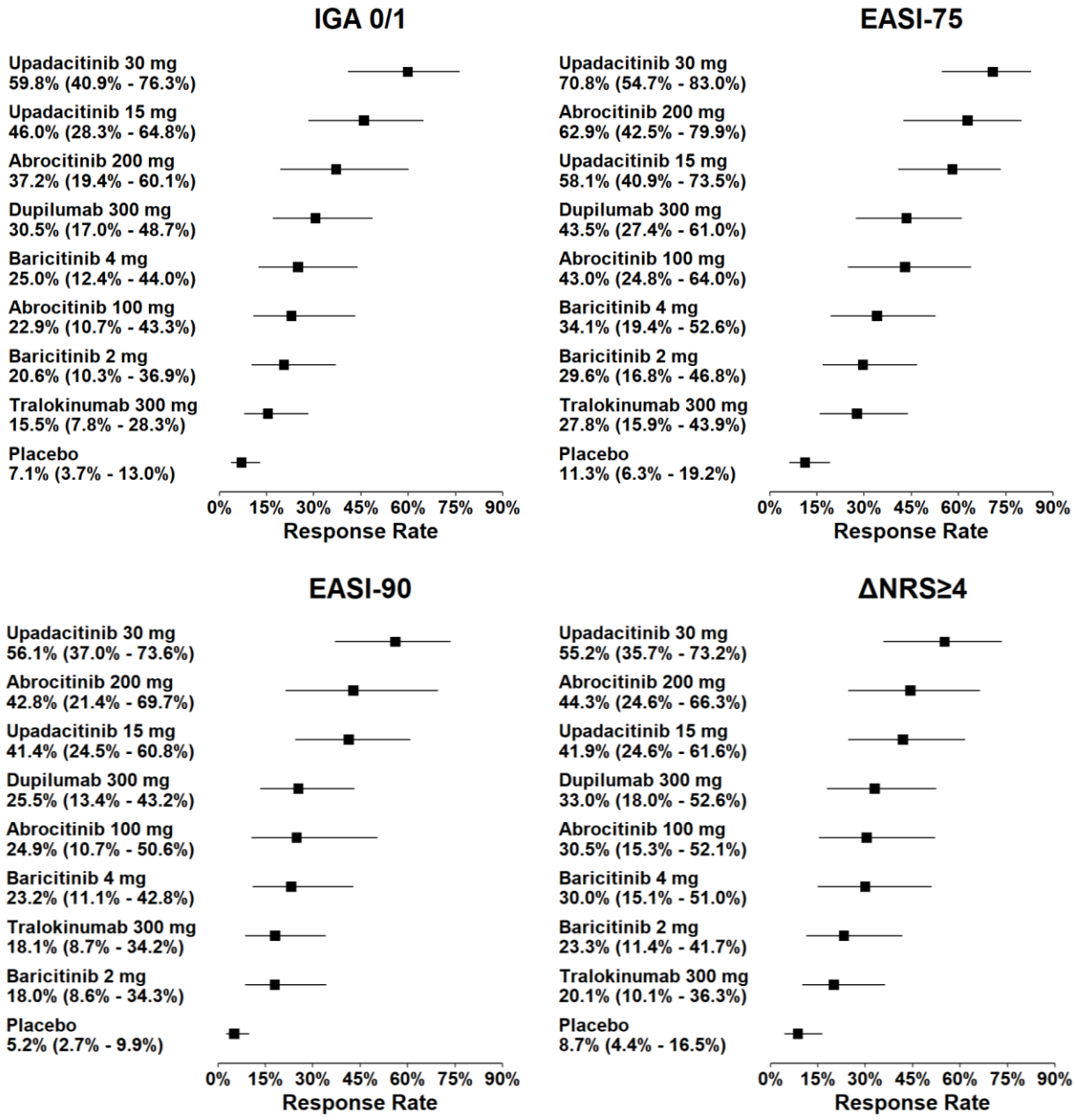
		Abrocitinib		Baricitinib			Dupilumab		Tralokinumab		Upadacitinib	
		JADE MONO-1	**JADE MONO-2**	**BREEZE-AD 1**	**BREEZE-AD 2**	**BREEZE-AD 5**	**SOLO 1**	**SOLO 2**	**ECZTRA 1**	**ECZTRA 2**	**Measure Up 1**	**Measure Up 2**
1	**Was randomization carried out appropriately?**	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Was the concealment of treatment allocation adequate?	Yes	Not clear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	**Were the groups similar at the outset of the study in terms of prognostic factors?**	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	Yes	Yes	Yes	Yes
4	**Were the care providers, participants, and outcome assessors blind to treatment allocation?**	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	**Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?**	No	Yes[b]	Yes	Yes	No	Yes	Yes	No	Yes[b]	No	No
		N/A	No	Yes	Yes		Yes	Yes		No		

Table S2. Complete quality assessment of each identified clinical study (continued)

		Abrocitinib (continued)		Baricitinib (continued)			Dupilumab (continued)		Tralokinumab (continued)		Upadacitinib (continued)	
		JADE MONO-1	**JADE MONO-2**	**BREEZE -AD 1**	**BREEZE -AD 2**	**BREEZE -AD 5**	**SOLO 1**	**SOLO 2**	**ECZTRA 1**	**ECZTRA 2**	**Measure Up 1**	**Measure Up 2**
6	**Is there any evidence to suggest that the authors measured more outcomes than they reported?**	No	Yes	No	No	No	No	No	No	No	NA[c]	NA[c]
7	**Did the analysis include an ITT analysis? If so, was this appropriate and were appropriate methods used to account for missing data?**	Yes Yes Yes	No	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes

[a]Hospital Anxiety and Depression Scale-Anxiety score was a bit varied
[b]More patients were reported to have dropped out of placebo group; however, a clear explanation was not provided
[c]No publication
ITT, Intention-to-treat

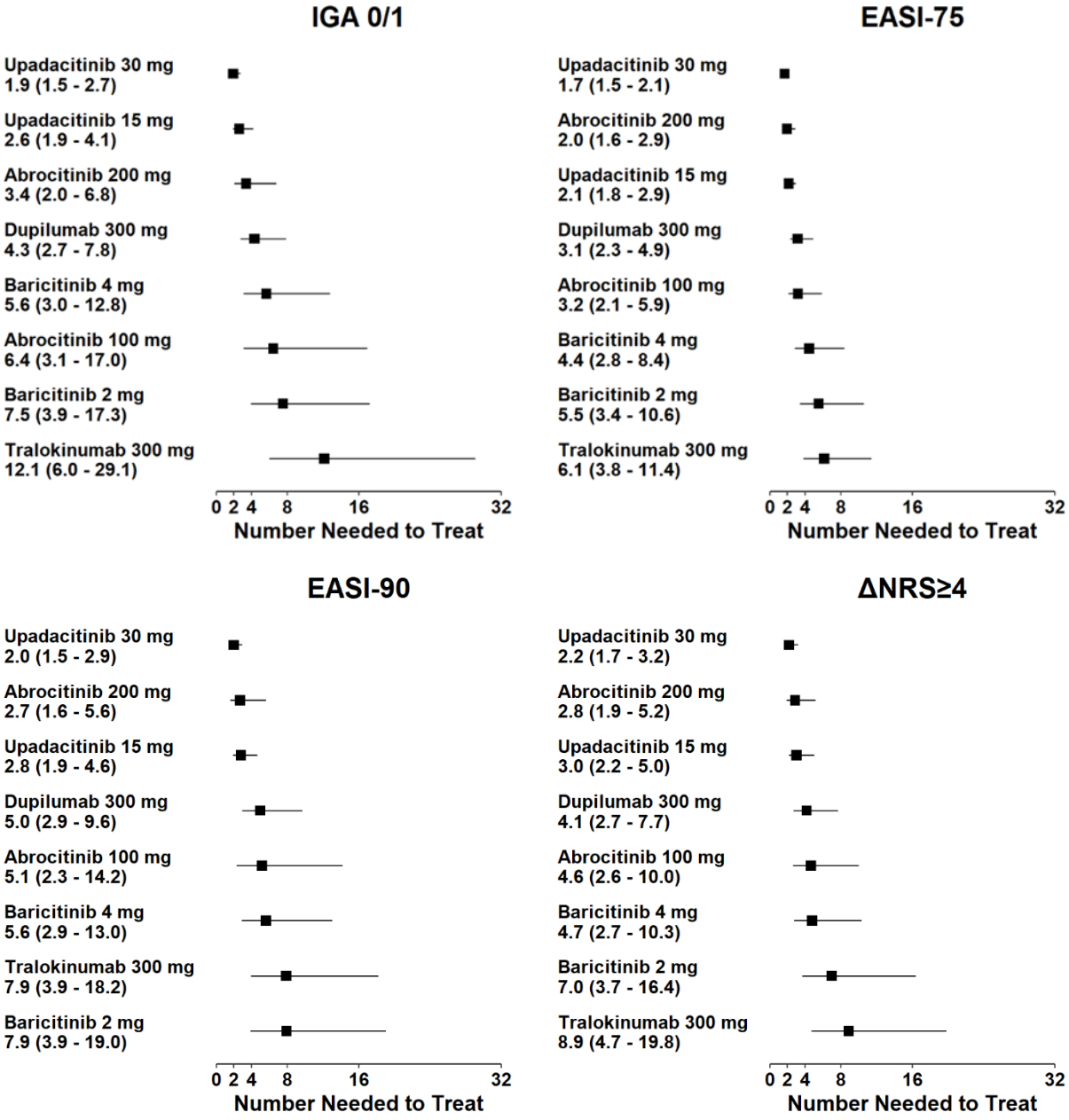
Figure S2. Response rate at primary endpoint evaluation (NMA fixed effects results)



Note: Higher values indicated higher efficacy. Endpoints were measured at the primary endpoint timepoint for each trial (week 12 for abrocitinib, week 16 for all other targeted therapies). Fixed effects models used for results estimation.

ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment for Atopic Dermatitis; NMA, Network meta-analysis

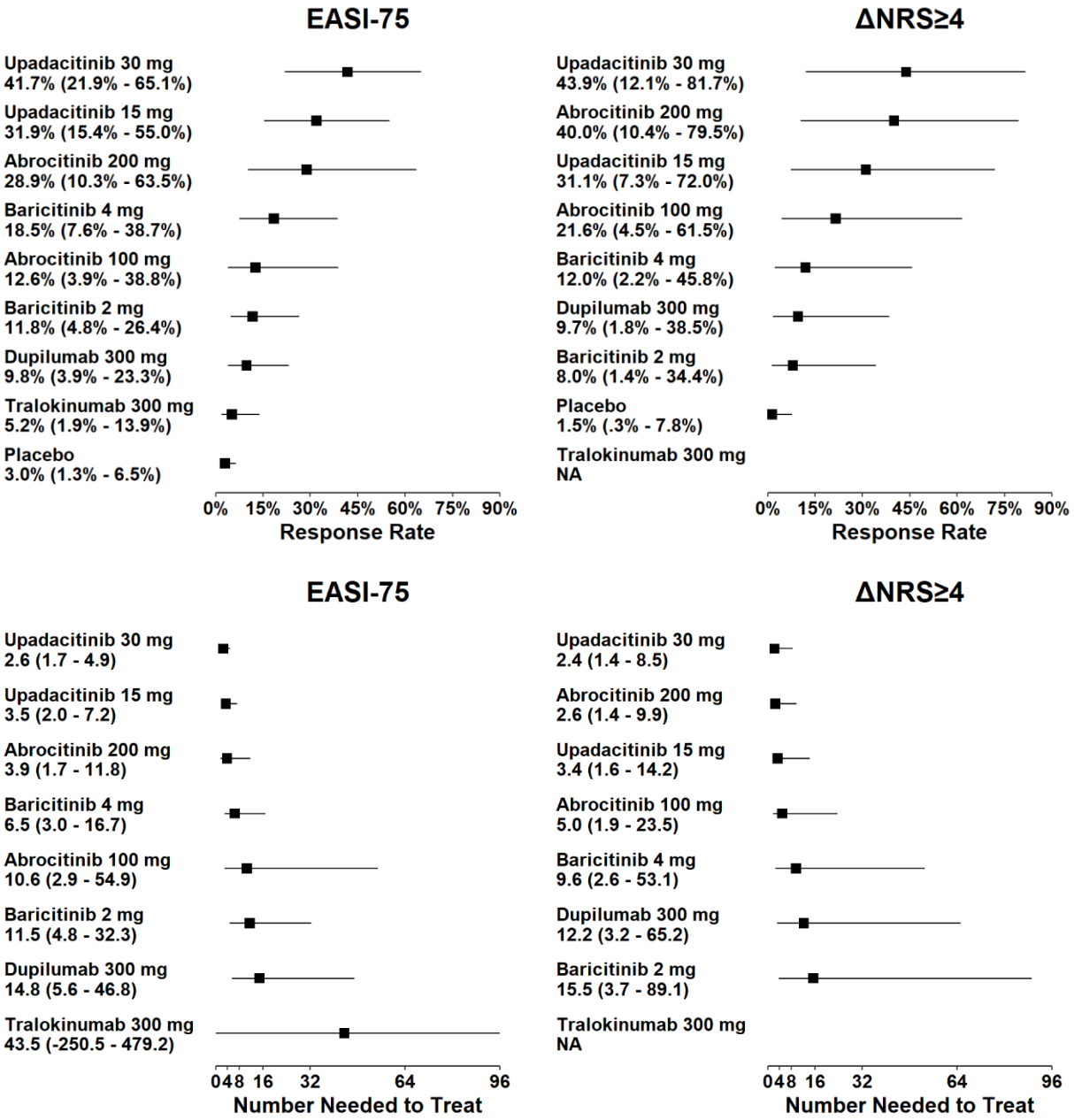
Figure S3. NNT at primary endpoint evaluation (NMA fixed effects results)



Note: Lower values indicated higher efficacy. Endpoints were measured the primary endpoint timepoint for each trial (week 12 for abrocitinib, week 16 for all other targeted therapies). Fixed effects models used for results estimation.

ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment for Atopic Dermatitis; NMA, Network meta-analysis; NNT, Number needed-to-treat

Figure S4. Week 2 response rate and NNT of EASI-75 and Change in Pruritus NRS score (ΔNRS≥4) (NMA fixed effects results for EASI-75; fixed effects baseline risk-adjusted results for ΔNRS≥4)



Note: Higher efficacy is indicated by higher values for response rate and lower values for NNT. Targeted therapy outcomes were reported at week 2 for all treatments except tralokinumab, which did not report ΔNRS≥4 at week 2. Fixed effects model used for EASI-75 results estimation. Fixed effects baseline risk-adjusted model used for ΔNRS≥4 results.

ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment for Atopic Dermatitis; NMA, Network meta-analysis; NRS, Numerical Rating Scale

Table S3. Odds ratios for IGA, EASI-75, EASI-90, and ΔNRS≥4 at primary endpoint timepoint

IGA 0/1

Comparator \ Treatment	Upadacitinib 30 mg	Upadacitinib 15 mg	Abrocitinib 200 mg	Dupilumab 300 mg	Baricitinib 4 mg	Abrocitinib 100 mg	Baricitinib 2 mg	Tralokinumab 300 mg	Placebo
Placebo	**19.47** (13.57, 28.75)	**11.12** (7.77, 16.41)	**7.71** (4.30, 14.95)	**5.75** (4.01, 8.39)	**4.38** (2.58, 7.47)	**3.88** (2.14, 7.58)	**3.39** (2.16, 5.41)	**2.39** (1.67, 3.52)	
Tralokinumab 300 mg	**8.14** (4.80, 13.85)	**4.65** (2.74, 7.91)	**3.23** (1.59, 6.84)	**2.40** (1.42, 4.06)	1.83 (0.95, 3.48)	1.62 (0.79, 3.47)	1.42 (0.78, 2.55)		**0.42** (0.28, 0.60)
Baricitinib 2 mg	**5.75** (3.18, 10.40)	**3.29** (1.82, 5.95)	**2.28** (1.07, 5.07)	1.70 (0.94, 3.05)	1.29 (0.79, 2.11)	1.15 (0.54, 2.56)		0.71 (0.39, 1.28)	**0.30** (0.18, 0.46)
Abrocitinib 100 mg	**5.02** (2.34, 10.24)	**2.87** (1.34, 5.84)	**1.99** (1.42, 2.81)	1.48 (0.69, 3.01)	1.12 (0.48, 2.52)		0.87 (0.39, 1.87)	0.62 (0.29, 1.26)	**0.26** (0.13, 0.47)
Baricitinib 4 mg	**4.46** (2.34, 8.54)	**2.55** (1.34, 4.88)	1.77 (0.80, 4.10)	1.32 (0.69, 2.51)		0.89 (0.40, 2.07)	0.78 (0.47, 1.27)	0.55 (0.29, 1.05)	**0.23** (0.13, 0.39)
Dupilumab 300 mg	**3.39** (2.01, 5.74)	**1.94** (1.15, 3.28)	1.34 (0.67, 2.85)		0.76 (0.40, 1.45)	0.67 (0.33, 1.44)	0.59 (0.33, 1.06)	**0.42** (0.25, 0.70)	**0.17** (0.12, 0.25)
Abrocitinib 200 mg	**2.52** (1.19, 5.11)	1.44 (0.68, 2.92)		0.75 (0.35, 1.50)	0.57 (0.24, 1.25)	**0.50** (0.36, 0.70)	**0.44** (0.20, 0.93)	**0.31** (0.15, 0.63)	**0.13** (0.07, 0.23)
Upadacitinib 15 mg	**1.75** (1.38, 2.22)		0.69 (0.34, 1.47)	**0.52** (0.30, 0.87)	**0.39** (0.20, 0.75)	**0.35** (0.17, 0.75)	**0.30** (0.17, 0.55)	**0.22** (0.13, 0.36)	**0.09** (0.06, 0.13)
Upadacitinib 30 mg		**0.57** (0.45, 0.72)	**0.40** (0.20, 0.84)	**0.30** (0.17, 0.50)	**0.22** (0.12, 0.43)	**0.20** (0.10, 0.43)	**0.17** (0.10, 0.32)	**0.12** (0.07, 0.21)	**0.05** (0.04, 0.07)

Asterisks indicate significance (odds ratio credible intervals do not cross 1)

EASI-75

Comparator \ Treatment	Upadacitinib 30 mg	Abrocitinib 200 mg	Upadacitinib 15 mg	Dupilumab 300 mg	Abrocitinib 100 mg	Baricitinib 4 mg	Baricitinib 2 mg	Tralokinumab 300 mg	Placebo
Placebo	**19.08** (14.14, 26.02)	**13.27** (7.80, 24.05)	**10.89** (8.16, 14.71)	**6.05** (4.38, 8.44)	**5.93** (3.49, 10.72)	**4.07** (2.64, 6.31)	**3.31** (2.27, 4.87)	**3.02** (2.19, 4.24)	
Tralokinumab 300 mg	**6.32** (4.02, 9.89)	**4.40** (2.34, 8.60)	**3.60** (2.31, 5.61)	**2.00** (1.25, 3.18)	**1.96** (1.05, 3.84)	1.34 (0.78, 2.32)	1.09 (0.66, 1.81)		**0.33** (0.24, 0.46)
Baricitinib 2 mg	**5.77** (3.53, 9.37)	**4.01** (2.08, 8.08)	**3.30** (2.03, 5.31)	**1.83** (1.10, 3.02)	1.79 (0.93, 3.60)	1.23 (0.81, 1.86)		0.91 (0.55, 1.51)	**0.30** (0.20, 0.44)
Baricitinib 4 mg	**4.70** (2.76, 7.97)	**3.27** (1.64, 6.79)	**2.68** (1.58, 4.53)	1.49 (0.86, 2.56)	1.46 (0.73, 3.02)		0.81 (0.54, 1.24)	0.74 (0.43, 1.29)	**0.25** (0.16, 0.38)
Abrocitinib 100 mg	**3.22** (1.66, 5.94)	**2.24** (1.63, 3.09)	1.84 (0.95, 3.37)	1.02 (0.52, 1.91)		0.69 (0.33, 1.37)	0.56 (0.28, 1.07)	**0.51** (0.26, 0.96)	**0.17** (0.09, 0.29)
Dupilumab 300 mg	**3.16** (2.01, 4.94)	**2.20** (1.17, 4.29)	**1.80** (1.16, 2.80)		0.98 (0.52, 1.91)	0.67 (0.39, 1.16)	**0.55** (0.33, 0.91)	**0.50** (0.31, 0.80)	**0.16** (0.12, 0.23)
Upadacitinib 15 mg	**1.75** (1.35, 2.28)	1.22 (0.66, 2.35)		**0.56** (0.36, 0.86)	0.54 (0.30, 1.05)	**0.37** (0.22, 0.63)	**0.30** (0.19, 0.49)	**0.28** (0.18, 0.43)	**0.09** (0.07, 0.12)
Abrocitinib 200 mg	1.44 (0.74, 2.66)		0.82 (0.43, 1.51)	**0.46** (0.23, 0.85)	**0.45** (0.32, 0.61)	**0.31** (0.15, 0.61)	**0.25** (0.12, 0.48)	**0.23** (0.12, 0.43)	**0.07** (0.04, 0.13)
Upadacitinib 30 mg		0.70 (0.38, 1.35)	**0.57** (0.44, 0.74)	**0.32** (0.20, 0.50)	**0.31** (0.17, 0.60)	**0.21** (0.12, 0.36)	**0.17** (0.11, 0.28)	**0.16** (0.10, 0.25)	**0.05** (0.04, 0.07)

Asterisks indicate significance (odds ratio credible intervals do not cross 1)

EASI-90

Comparator \ Treatment	Upadacitinib 30 mg	Abrocitinib 200 mg	Upadacitinib 15 mg	Dupilumab 300 mg	Abrocitinib 100 mg	Baricitinib 4 mg	Tralokinumab 300 mg	Baricitinib 2 mg	Placebo
Placebo	**23.17** (16.07, 34.06)	**13.49** (6.51, 33.31)	**12.84** (8.93, 18.88)	**6.20** (4.19, 9.41)	**5.98** (2.84, 14.92)	**5.50** (3.11, 9.94)	**3.98** (2.51, 6.73)	**3.98** (2.40, 6.79)	
Baricitinib 2 mg	**5.82** (3.04, 10.98)	**3.40** (1.37, 9.51)	**3.22** (1.69, 6.07)	1.56 (0.81, 2.99)	1.50 (0.60, 4.25)	1.38 (0.82, 2.31)	1.00 (0.49, 2.08)		**0.25** (0.15, 0.42)
Tralokinumab 300 mg	**5.81** (3.07, 10.60)	**3.39** (1.38, 9.27)	**3.22** (1.70, 5.88)	1.55 (0.81, 2.90)	1.50 (0.60, 4.13)	1.37 (0.64, 2.93)		1.00 (0.48, 2.03)	**0.25** (0.15, 0.40)
Baricitinib 4 mg	**4.22** (2.10, 8.38)	2.47 (0.96, 7.12)	**2.34** (1.17, 4.64)	1.13 (0.56, 2.28)	1.09 (0.42, 3.18)		0.73 (0.34, 1.57)	0.72 (0.43, 1.22)	**0.18** (0.10, 0.32)
Abrocitinib 100 mg	**3.87** (1.46, 8.96)	**2.26** (1.59, 3.23)	2.14 (0.81, 4.97)	1.03 (0.39, 2.44)		0.92 (0.32, 2.39)	0.67 (0.24, 1.66)	0.66 (0.23, 1.67)	**0.17** (0.07, 0.35)
Dupilumab 300 mg	**3.73** (2.15, 6.48)	2.18 (0.94, 5.78)	**2.07** (1.19, 3.59)		0.97 (0.41, 2.59)	0.88 (0.44, 1.79)	0.64 (0.34, 1.23)	0.64 (0.33, 1.24)	**0.16** (0.11, 0.24)
Upadacitinib 15 mg	**1.80** (1.42, 2.30)	1.05 (0.46, 2.76)		**0.48** (0.28, 0.84)	0.47 (0.20, 1.24)	**0.43** (0.22, 0.86)	**0.31** (0.17, 0.59)	**0.31** (0.16, 0.59)	**0.08** (0.05, 0.11)
Abrocitinib 200 mg	1.71 (0.65, 3.91)		0.95 (0.36, 2.17)	0.46 (0.17, 1.07)	**0.44** (0.31, 0.63)	0.41 (0.14, 1.05)	**0.30** (0.11, 0.72)	**0.29** (0.10, 0.73)	**0.07** (0.03, 0.15)
Upadacitinib 30 mg		0.58 (0.26, 1.53)	**0.55** (0.44, 0.70)	**0.27** (0.15, 0.47)	**0.26** (0.11, 0.69)	**0.24** (0.12, 0.48)	**0.17** (0.09, 0.33)	**0.17** (0.09, 0.33)	**0.04** (0.03, 0.06)

Asterisks indicate significance (odds ratio credible intervals do not cross 1)

ΔNRS≥4

Comparator \ Treatment	Upadacitinib 30 mg	Abrocitinib 200 mg	Upadacitinib 15 mg	Dupilumab 300 mg	Abrocitinib 100 mg	Baricitinib 4 mg	Baricitinib 2 mg	Tralokinumab 300 mg	Placebo
Placebo	**12.88** (9.42, 17.94)	**8.30** (5.03, 14.38)	**7.56** (5.53, 10.53)	**5.16** (3.63, 7.44)	**4.59** (2.78, 7.95)	**4.49** (2.71, 7.50)	**3.17** (2.03, 5.04)	**2.64** (1.86, 3.84)	
Tralokinumab 300 mg	**4.88** (3.01, 7.87)	**3.15** (1.68, 6.02)	**2.87** (1.77, 4.62)	**1.95** (1.17, 3.25)	1.74 (0.93, 3.33)	1.70 (0.91, 3.16)	1.20 (0.67, 2.14)		**0.38** (0.26, 0.54)
Baricitinib 2 mg	**4.06** (2.32, 7.07)	**2.62** (1.32, 5.30)	**2.39** (1.36, 4.16)	1.62 (0.91, 2.89)	1.45 (0.73, 2.93)	1.41 (0.88, 2.28)		0.83 (0.47, 1.49)	**0.32** (0.20, 0.49)
Baricitinib 4 mg	**2.87** (1.57, 5.24)	1.85 (0.90, 3.88)	1.69 (0.92, 3.08)	1.15 (0.62, 2.13)	1.02 (0.50, 2.14)		0.71 (0.44, 1.14)	0.59 (0.32, 1.10)	**0.22** (0.13, 0.37)
Abrocitinib 100 mg	**2.80** (1.50, 5.12)	**1.81** (1.32, 2.49)	1.65 (0.88, 3.00)	1.12 (0.58, 2.08)		0.98 (0.47, 2.00)	0.69 (0.34, 1.37)	0.57 (0.30, 1.08)	**0.22** (0.13, 0.36)
Dupilumab 300 mg	**2.50** (1.54, 4.05)	1.61 (0.87, 3.09)	1.47 (0.91, 2.38)		0.89 (0.48, 1.71)	0.87 (0.47, 1.62)	0.62 (0.35, 1.10)	**0.51** (0.31, 0.85)	**0.19** (0.13, 0.28)
Upadacitinib 15 mg	**1.70** (1.34, 2.16)	1.10 (0.60, 2.06)		0.68 (0.42, 1.10)	0.61 (0.33, 1.14)	0.59 (0.32, 1.08)	**0.42** (0.24, 0.74)	**0.35** (0.22, 0.57)	**0.13** (0.10, 0.18)
Abrocitinib 200 mg	1.55 (0.83, 2.83)		0.91 (0.49, 1.66)	0.62 (0.32, 1.15)	**0.55** (0.40, 0.76)	0.54 (0.26, 1.11)	**0.38** (0.19, 0.76)	**0.32** (0.17, 0.60)	**0.12** (0.07, 0.20)
Upadacitinib 30 mg		0.64 (0.35, 1.21)	**0.59** (0.46, 0.74)	**0.40** (0.25, 0.65)	**0.36** (0.20, 0.67)	**0.35** (0.19, 0.64)	**0.25** (0.14, 0.43)	**0.20** (0.13, 0.33)	**0.08** (0.06, 0.11)

Asterisks indicate significance (odds ratio credible intervals do not cross 1)

ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment for Atopic Dermatitis

Table S4. Odds ratios for EASI-75 and ΔNRS≥4 at week 2

EASI-75

Comparator \ Treatment	Upadacitinib 30 mg	Upadacitinib 15 mg	Abrocitinib 200 mg	Baricitinib 4 mg	Abrocitinib 100 mg	Baricitinib 2 mg	Dupilumab 300 mg	Tralokinumab 300 mg	Placebo
Placebo	**23.20** (14.72, 38.84)	**15.18** (9.59, 25.47)	**13.02** (5.13, 44.86)	**7.37** (4.08, 13.76)	**4.65** (1.75, 16.36)	**4.32** (2.52, 7.68)	**3.54** (2.00, 6.64)	1.78 (0.95, 3.65)	
Tralokinumab 300 mg	**13.04** (5.59, 29.31)	**8.52** (3.65, 19.17)	**7.34** (2.26, 29.39)	**4.13** (1.64, 10.00)	2.62 (0.78, 10.68)	2.43 (0.99, 5.66)	1.99 (0.80, 4.81)		0.56 (0.27, 1.05)
Dupilumab 300 mg	**6.56** (3.02, 14.13)	**4.30** (1.97, 9.26)	**3.69** (1.19, 14.39)	2.08 (0.88, 4.86)	1.32 (0.41, 5.25)	1.22 (0.53, 2.75)		0.50 (0.21, 1.25)	**0.28** (0.15, 0.50)
Baricitinib 2 mg	**5.37** (2.58, 11.29)	**3.51** (1.69, 7.40)	**3.03** (1.00, 11.44)	**1.70** (1.01, 2.90)	1.08 (0.35, 4.17)		0.82 (0.36, 1.87)	0.41 (0.18, 1.01)	**0.23** (0.13, 0.40)
Abrocitinib 100 mg	**4.99** (1.32, 14.91)	3.27 (0.86, 9.76)	**2.80** (1.79, 4.45)	1.57 (0.40, 5.08)		0.92 (0.24, 2.89)	0.76 (0.19, 2.42)	0.38 (0.09, 1.28)	**0.22** (0.06, 0.57)
Baricitinib 4 mg	**3.15** (1.45, 6.88)	2.06 (0.95, 4.52)	1.78 (0.57, 6.88)		0.64 (0.20, 2.51)	**0.59** (0.34, 0.99)	0.48 (0.21, 1.14)	**0.24** (0.10, 0.61)	**0.14** (0.07, 0.24)
Abrocitinib 200 mg	1.78 (0.48, 5.14)	1.17 (0.32, 3.37)		0.56 (0.14, 1.75)	**0.36** (0.22, 0.56)	**0.33** (0.09, 1.00)	**0.27** (0.07, 0.84)	**0.14** (0.03, 0.44)	**0.08** (0.02, 0.20)
Upadacitinib 15 mg	**1.53** (1.20, 1.94)		0.86 (0.30, 3.18)	0.48 (0.22, 1.05)	0.31 (0.10, 1.16)	**0.28** (0.14, 0.59)	**0.23** (0.11, 0.51)	**0.12** (0.05, 0.27)	**0.07** (0.04, 0.10)
Upadacitinib 30 mg		**0.65** (0.52, 0.83)	0.56 (0.20, 2.08)	**0.32** (0.14, 0.69)	**0.20** (0.07, 0.76)	**0.19** (0.09, 0.39)	**0.15** (0.07, 0.33)	**0.08** (0.03, 0.18)	**0.04** (0.03, 0.07)

Asterisks indicate significance (odds ratio credible intervals do not cross 1)

ΔNRS≥4

Comparator \ Treatment	Upadacitinib 30 mg	Abrocitinib 200 mg	Upadacitinib 15 mg	Abrocitinib 100 mg	Baricitinib 4 mg	Dupilumab 300 mg	Baricitinib 2 mg	Placebo
Placebo	**52.15** (43.52, 63.29)	**44.43** (34.17, 59.58)	**30.09** (24.72, 36.90)	**18.34** (13.47, 25.30)	**9.15** (5.28, 15.49)	**7.18** (5.12, 9.79)	**5.85** (3.53, 9.01)	
Baricitinib 2 mg	**8.92** (5.47, 15.85)	**7.60** (4.40, 14.56)	**5.14** (3.13, 9.15)	**3.13** (1.77, 6.08)	1.57 (0.93, 2.67)	1.23 (0.71, 2.23)		**0.17** (0.11, 0.28)
Dupilumab 300 mg	**7.27** (5.09, 10.72)	**6.20** (4.14, 9.66)	**4.20** (2.91, 6.21)	**2.56** (1.66, 4.06)	1.28 (0.68, 2.40)		0.81 (0.45, 1.42)	**0.14** (0.10, 0.20)
Baricitinib 4 mg	**5.71** (3.18, 10.52)	**4.87** (2.56, 9.64)	**3.29** (1.83, 6.11)	**2.01** (1.03, 4.03)		0.78 (0.42, 1.48)	0.64 (0.37, 1.07)	**0.11** (0.06, 0.19)
Abrocitinib 100 mg	**2.84** (2.01, 4.02)	**2.43** (1.70, 3.47)	**1.64** (1.15, 2.33)		**0.50** (0.25, 0.97)	**0.39** (0.25, 0.60)	**0.32** (0.16, 0.56)	**0.06** (0.04, 0.07)
Upadacitinib 15 mg	**1.73** (1.36, 2.22)	**1.48** (1.08, 2.05)		**0.61** (0.43, 0.87)	**0.30** (0.16, 0.55)	**0.24** (0.16, 0.34)	**0.19** (0.11, 0.32)	**0.03** (0.03, 0.04)
Abrocitinib 200 mg	1.17 (0.85, 1.59)		**0.68** (0.49, 0.93)	**0.41** (0.29, 0.59)	**0.21** (0.10, 0.39)	**0.16** (0.10, 0.24)	**0.13** (0.07, 0.23)	**0.02** (0.02, 0.03)
Upadacitinib 30 mg		0.85 (0.63, 1.17)	**0.58** (0.45, 0.74)	**0.35** (0.25, 0.50)	**0.17** (0.10, 0.31)	**0.14** (0.09, 0.20)	**0.11** (0.06, 0.18)	**0.02** (0.02, 0.02)

Asterisks indicate significance (odds ratio credible intervals do not cross 1)

ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index

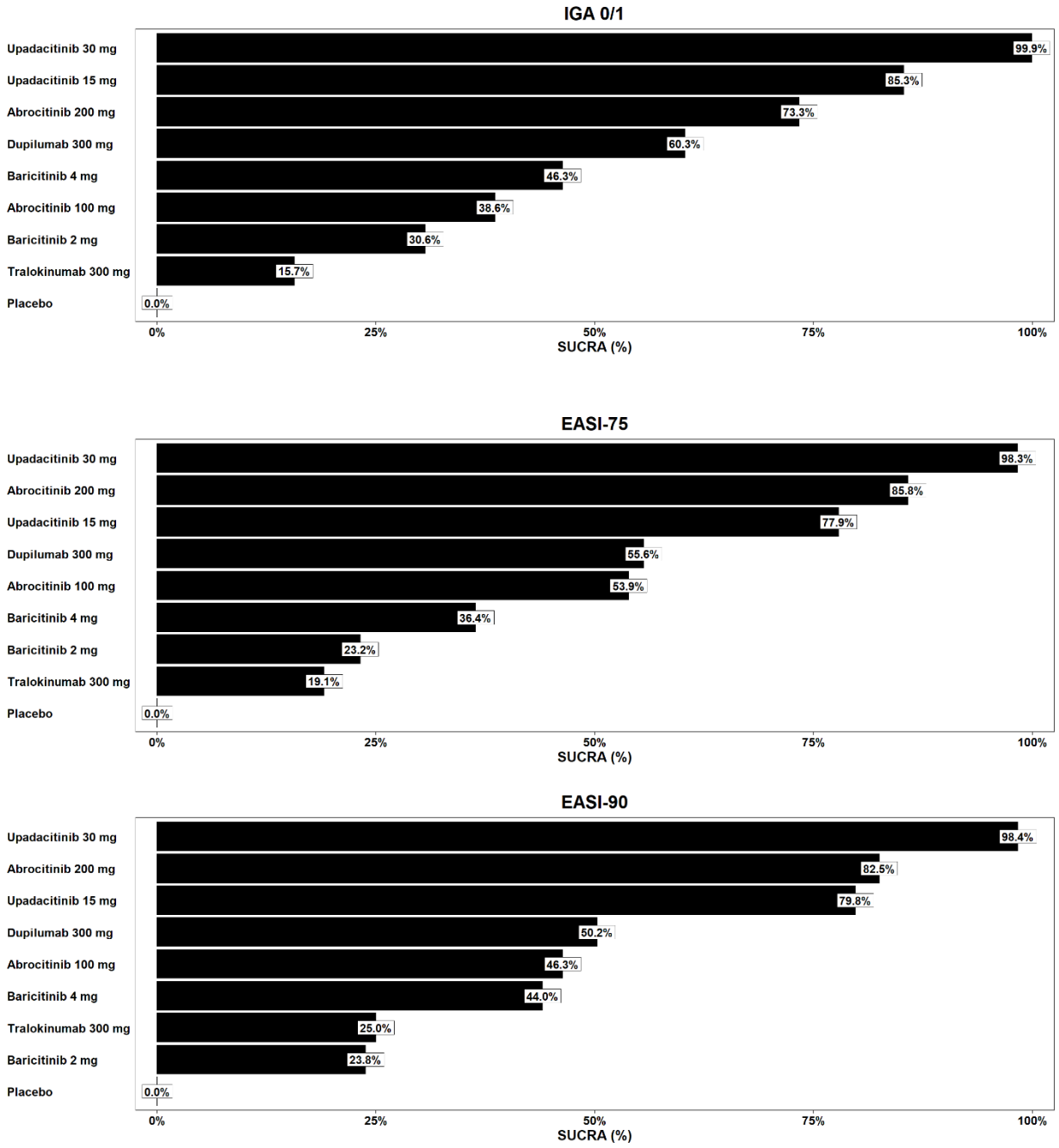
Table S5. Overview of results for the network meta-analysis at week 2

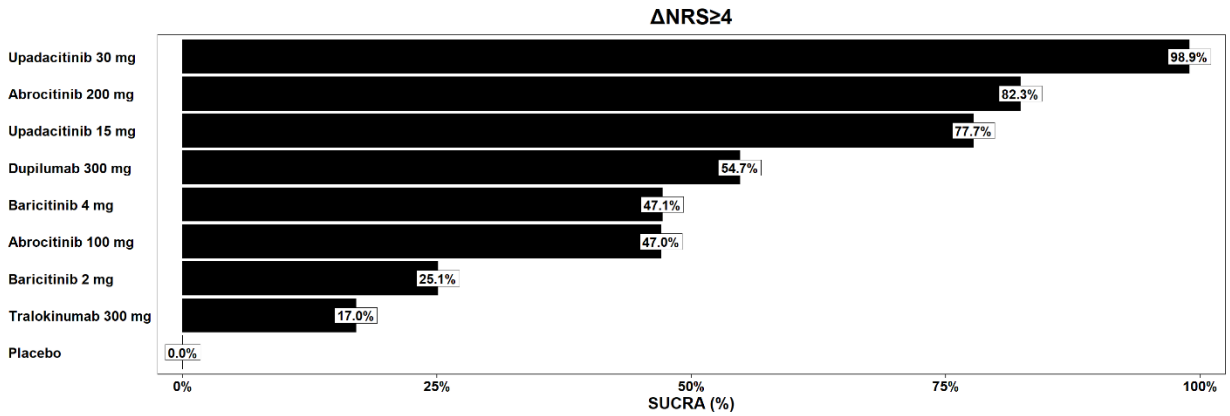
			Response rate observed in study at week 2, %	
Study	**Treatment**	**N**	**EASI-75**	**ΔNRS≥4**
JADE MONO-1	Abrocitinib 200mg	154	24.0%	45.6%
	Abrocitinib 100mg	156	10.3%	20.4%
	Placebo	77	3.9%	2.7%
JADE MONO-2	Abrocitinib 200mg	155	24.3%	35.3%
	Abrocitinib 100mg	158	10.2%	23.1%
	Placebo	78	1.3%	3.9%
BREEZE-AD1	Baricitinib 4mg	125	13.6%	15.9%
	Baricitinib 2mg	123	6.6%	8.0%
	Placebo	249	1.3%	0.0%
BREEZE-AD2	Baricitinib 4mg	123	17.2%	10.3%
	Baricitinib 2mg	123	12.9%	6.5%
	Placebo	244	3.5%	0.9%
BREEZE-AD5	Baricitinib 2mg	146	16.9%	12.1%
	Placebo	147	4.8%	1.6%
SOLO 1	Dupilumab 300mg	224		9.4%
	Placebo	224		3.3%
SOLO 2	Dupilumab 300mg	233		10.7%
	Placebo	236		0.9%
SOLO pooled[a]	Dupilumab 300mg	457	10.5%	
	Placebo	460	3.3%	
ECZTRA 1[b]	Tralokinumab 300mg	603	4.7%	
	Placebo	199	4.5%	
ECZTRA 2 [b]	Tralokinumab 300mg	593	4.7%	
	Placebo	201	1.1%	
MEASURE UP 1	Upadacitinib 30mg	285	47.4%	48.2%
	Upadacitinib 15mg	281	38.1%	32.5%
	Placebo	281	3.6%	2.2%
MEASURE UP 2	Upadacitinib 30mg	282	44.0%	39.3%
	Upadacitinib 15mg	276	33.0%	30.0%
	Placebo	278	3.6%	2.2%

[a]Data from SOLO 1 and SOLO 2 were pooled for analysis for EASI-75 as reported in Thaçi et al., 2019 [9]
[b]ECZTRA 1 and ECZTRA 2 did not report ΔNRS≥4 at week 2

ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index

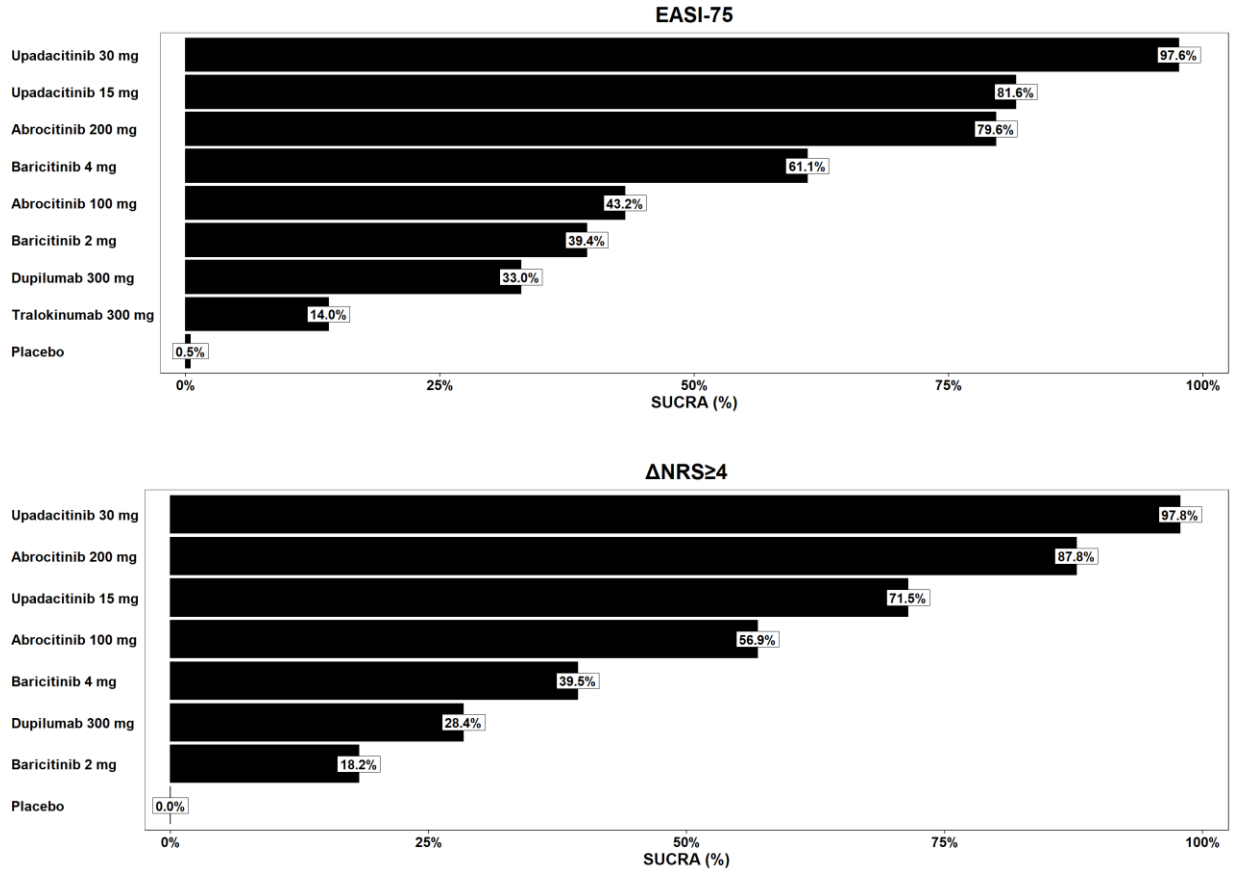
Figure S5. SUCRA scores for IGA, EASI-75, EASI-90, and ΔNRS≥4 at primary endpoint timepoint





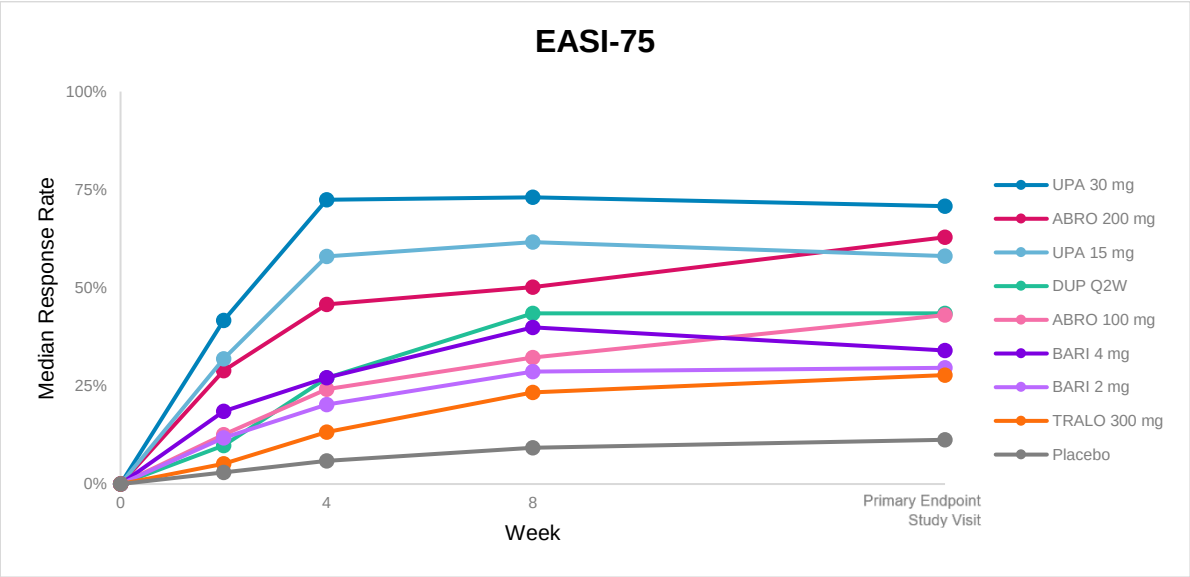
Note: SUCRA scores are based on the overall ranking of a treatment from the NMA, with higher SUCRA scores indicating a greater likelihood that a treatment is the top ranked treatment in the network.
ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment for Atopic Dermatitis; SUCRA, surface under the cumulative ranking curve

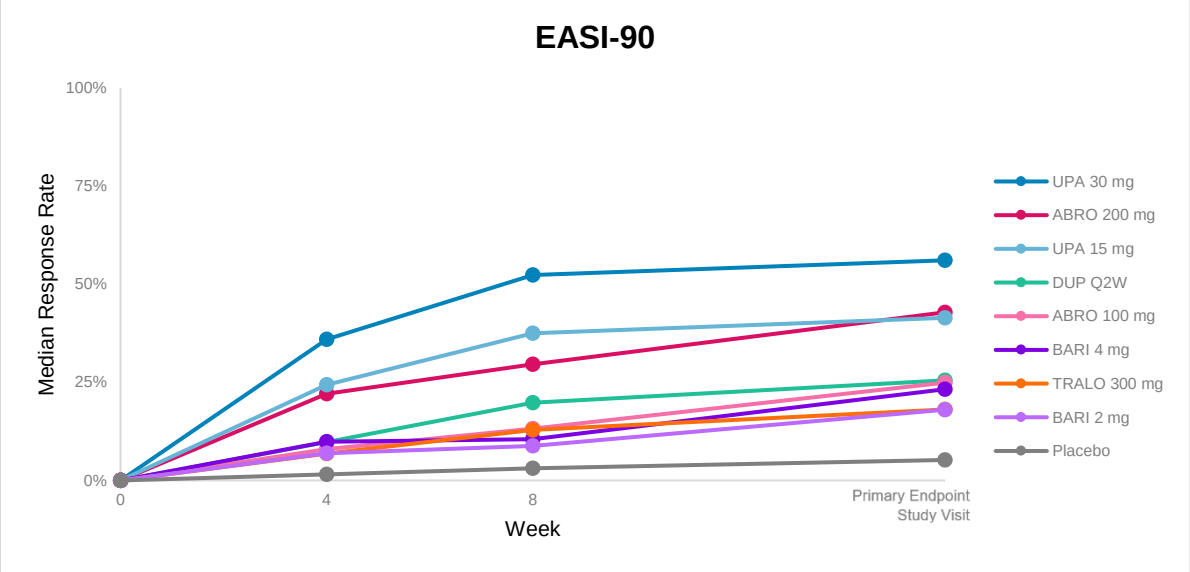
Figure S6. SUCRA scores for EASI-75 and ΔNRS≥4 at week 2

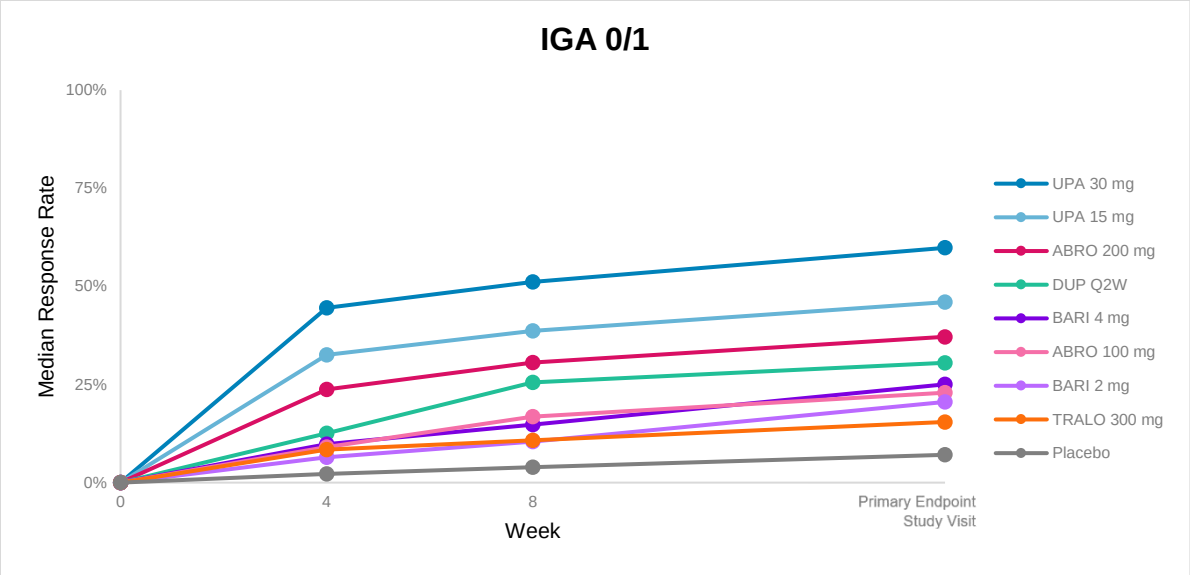


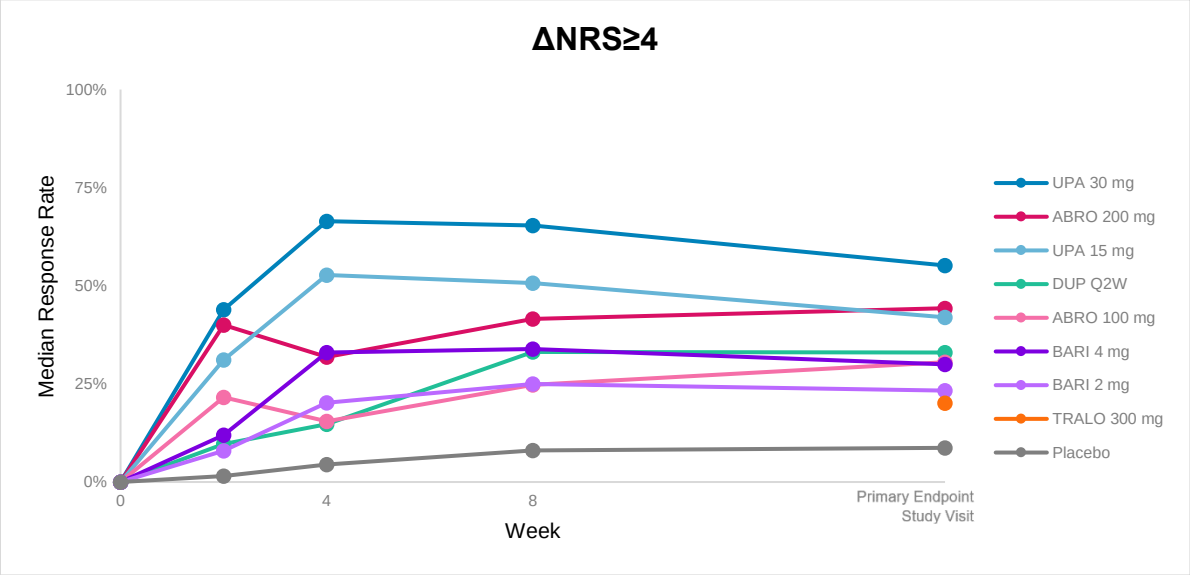
Note: SUCRA scores are based on the overall ranking of a treatment from the NMA, with higher SUCRA scores indicating a greater likelihood that a treatment is the top ranked treatment in the network.
ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; SUCRA, surface under the cumulative ranking curve

Figure S7. Longitudinal Assessment of All Efficacy Outcomes Through the Primary Endpoint Study Visit (Bayesian NMA Fixed Effects Results)









Primary endpoint study visit was at Week 12 for abrocitinib trials (JADE MONO-1, JADE MONO-2) and Week 16 for all other targeted therapies.

ΔNRS≥4, Worst Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; ABRO, abrocitinib; BARI, baricitinib; DUPI, dupilumab; IGA, Investigator Global Assessment for Atopic Dermatitis; NMA, network meta-analysis; NNT, number needed to treat; TRALO, tralokinumab; UPA, upadacitinib.

Table S6. SUCRA, Response Rate, OR, and NNT for All Efficacy Outcomes at Week 4 (Bayesian NMA Fixed Effects Results)

Endpoint	Treatment	N[a]	SUCRA	Response Rate, Median (95% CI)	Odds Ratio vs Placebo, Median (95% CI)	NNT vs. Placebo, Median (95% CI)
EASI-75[b]	ABRO 100mg	314	42.0%	24.2% (8.2%-53.2%)	5.1 (3.5-6.9)	5.5 (2.8-16.1)
	ABRO 200mg	309	74.9%	45.7% (19.1%-74.9%)	13.5 (9.5-17.7)	2.5 (1.7-5.8)
	BARI 2mg	392	27.7%	20.3% (6.7%-47.3%)	4.0 (3.1-5.4)	7.0 (3.3-20.8)
	BARI 4mg	248	52.1%	27.1% (9.3%-57.5%)	5.9 (4.1-8.8)	4.8 (2.5-13.6)
	DUPI Q2W	457	53.2%	27.0% (9.6%-56.4%)	5.9 (4.7-7.4)	4.8 (2.6-13.0)
	TRALO 300mg	1,196	12.6%	13.2% (4.2%-34.7%)	2.4 (2.0-3.0)	13.8 (5.8-43.2)
	UPA 15mg	557	87.5%	58.0% (28.4%-82.7%)	21.9 (18.0-26.5)	1.9 (1.5-3.8)
	UPA 30mg	567	100.0%	72.5% (43.1%-90.1%)	41.8 (33.8-51.3)	1.5 (1.4-2.4)
	Placebo	2,214	0.0%	5.9% (1.8%-17.7%)	—	—
EASI-90	ABRO 100mg	314	36.9%	8.0% (1.4%-38.4%)	5.3 (1.7-23.8)	16.2 (2.9-134.8)
	ABRO 200mg	309	78.8%	22.0% (4.7%-66.6%)	17.1 (5.9-75.3)	4.9 (1.6-24.7)
	BARI 2mg	246	29.7%	7.0% (1.5%-27.4%)	4.6 (2.0-11.7)	19.0 (4.4-111.9)
	BARI 4mg	248	48.1%	9.9% (2.3%-35.2%)	6.8 (3.1-16.6)	12.2 (3.3-59.7)
	DUPI Q2W	457	46.0%	9.8% (2.3%-34.3%)	6.7 (3.3-15.7)	12.3 (3.4-57.1)
	TRALO 300mg	1,196	31.8%	6.8% (1.4%-30.5%)	4.5 (1.8-15.2)	19.6 (3.8-137.9)
	UPA 15mg	557	81.0%	24.4% (7.0%-58.3%)	19.9 (11.6-37.4)	4.4 (1.9-15.3)
	UPA 30mg	567	97.6%	36.0% (11.6%-70.9%)	34.6 (20.3-65.0)	2.9 (1.5-9.0)
	Placebo	2,067	0.0%	1.6% (0.4%-5.8%)	—	—
IGA 0/1	ABRO 100mg	314	37.6%	9.1% (2.6%-29.9%)	4.4 (1.8-13.6)	14.9 (3.9-76.4)
	ABRO 200mg	309	76.6%	23.7% (7.9%-56.6%)	13.7 (5.8-41.4)	4.7 (1.9-15.0)
	BARI 2mg	392	21.0%	6.4% (2.2%-17.3%)	3.1 (1.7-5.6)	24.0 (7.9-92.1)
	BARI 4mg	248	42.9%	9.8% (3.4%-25.1%)	4.8 (2.7-9.1)	13.2 (4.9-42.7)
	DUPI Q2W	457	53.3%	12.6% (4.3%-32.1%)	6.3 (3.3-13.5)	9.7 (3.6-31.0)
	TRALO 300mg	1,196	35.0%	8.4% (2.5%-27.6%)	4.0 (1.7-12.1)	16.6 (4.2-84.6)
	UPA 15mg	557	84.4%	32.6% (13.7%-60.1%)	21.3 (12.1-41.3)	3.3 (1.8-7.9)
	UPA 30mg	567	99.2%	44.5% (21.0%-71.4%)	35.4 (20.2-68.5)	2.4 (1.5-5.0)

Table S6. SUCRA, Response Rate, OR, and NNT for All Efficacy Outcomes at Week 4 (Bayesian NMA Fixed Effects Results) (continued)

Endpoint (continued)	Treatment (continued)	N[a]	SUCRA (continued)	Response Rate, Median (95% CI) (continued)	Odds Ratio vs Placebo, Median (95% CI) (continued)	NNT vs. Placebo, Median (95% CI) (continued)
	Placebo	2,214	0.0%	2.2% (0.9%-5.4%)	—	—
∆NRS≥4	ABRO 100mg	314	25.5%	15.5% (3.4%-48.9%)	3.9 (2.3-7.2)	9.3 (3.1-45.1)
	ABRO 200mg	309	62.7%	31.8% (8.3%-70.9%)	10.0 (5.8-18.2)	3.7 (1.8-14.0)
	BARI 2mg	392	38.6%	20.2% (4.6%-57.0%)	5.4 (3.1-9.9)	6.4 (2.5-28.5)
	BARI 4mg	248	65.1%	33.0% (8.6%-72.2%)	10.6 (6.0-19.7)	3.5 (1.8-13.4)
	DUPI Q2W	457	22.9%	14.8% (3.3%-46.5%)	3.7 (2.4-6.0)	9.8 (3.4-44.9)
	TRALO 300mg		—	—	—	—
	UPA 15mg	557	85.3%	52.7% (18.2%-84.9%)	24.0 (15.5-38.9)	2.1 (1.5-5.9)
	UPA 30mg	567	100.0%	66.5% (28.3%-90.9%)	42.5 (27.4-69.2)	1.6 (1.3-3.7)
	Placebo	1,814	0.0%	4.4% (1.0%-17.9%)	—	—

[a] N represents sample size of trial arms used in the NMA
[b] Baseline-risk adjusted model was selected based on model fit statistics.

ΔNRS≥4, Worst Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; ABRO, abrocitinib; BARI, baricitinib; CI, credible interval; DUPI, dupilumab; IGA, Investigator Global Assessment for Atopic Dermatitis; NMA, network meta-analysis; NNT, number needed to treat; SUCRA, surface under the cumulative ranking curve; UPA, upadacitinib.

Table S7. SUCRA, Response Rate, OR, and NNT for All Efficacy Outcomes at Week 8 (Bayesian NMA Fixed Effects Results)

Endpoint	Treatment	N[a]	SUCRA	Response Rate, Median (95% CI)	Odds Ratio vs Placebo, Median (95% CI)	NNT vs. Placebo, Median (95% CI)
EASI-75	ABRO 100mg	314	35.6%	32.2% (16.0%-54.8%)	4.7 (2.8-8.1)	4.4 (2.5-9.6)
	ABRO 200mg	309	71.9%	50.2% (28.7%-72.0%)	9.9 (6.0-17.2)	2.5 (1.8-4.3)
	BARI 2mg	392	27.1%	28.6% (14.5%-48.8%)	4.0 (2.6-6.0)	5.2 (3.1-10.8)
	BARI 4mg	248	53.0%	39.9% (21.7%-61.6%)	6.5 (4.2-10.3)	3.3 (2.2-6.1)
	DUP Q2W	457	60.2%	43.5% (25.0%-64.1%)	7.6 (5.3-10.9)	2.9 (2.1-5.0)
	TRALO 300mg	1,196	15.6%	23.4% (11.7%-41.4%)	3.0 (2.1-4.3)	7.2 (4.0-15.3)
	UPA 15mg	557	86.6%	61.6% (41.5%-78.5%)	15.8 (11.6-21.8)	1.9 (1.6-2.7)
	UPA 30mg	567	100.0%	73.1% (54.3%-86.1%)	26.7 (19.3-37.2)	1.6 (1.4-2.0)
	Placebo	2,214	0.0%	9.2% (4.6%-17.8%)	--	--
EASI-90	ABRO 100mg	314	39.8%	13.2% (5.0%-32.9%)	4.8 (2.1-12.7)	10.0 (3.5-35.7)
	ABRO 200mg	309	76.0%	29.6% (13.0%-57.2%)	13.2 (6.1-34.6)	3.8 (1.9-9.2)
	BARI 2mg	246	21.3%	8.8% (3.6%-20.4%)	3.0 (1.5-6.3)	17.7 (6.3-74.8)
	BARI 4mg	248	30.4%	10.5% (4.4%-23.6%)	3.7 (1.9-7.5)	13.6 (5.3-45.2)
	DUP Q2W	457	59.5%	19.8% (9.4%-37.8%)	7.8 (4.5-14.5)	6.0 (3.0-13.5)
	TRALO 300mg	1,196	39.2%	12.9% (5.5%-28.8%)	4.7 (2.5-10.1)	10.3 (4.1-29.2)
	UPA 15mg	557	84.2%	37.5% (21.3%-57.7%)	18.9 (12.2-31.1)	2.9 (1.9-5.1)
	UPA 30mg	567	99.5%	52.3% (33.1%-71.4%)	34.6 (22.3-56.8)	2.0 (1.5-3.2)
	Placebo	2,067	0.0%	3.1% (1.6%-5.8%)	--	--
IGA 0/1[b]	ABRO 100mg	314	45.5%	16.8% (5.1%-42.8%)	5.0 (3.1-7.2)	7.8 (3.2 - 26.7)
	ABRO 200mg	309	73.1%	30.6% (10.6%-61.8%)	11.0 (6.8-15.1)	3.8 (2.0 - 10.8)
	BARI 2mg	392	19.4%	10.5% (3.1%-29.8%)	2.9 (2.0-4.2)	15.5 (5.5 - 56.1)
	BARI 4mg	248	39.5%	14.7% (4.5%-39.1%)	4.2 (2.8-6.6)	9.3 (3.6 - 31.9)
	DUP Q2W	457	64.6%	25.5% (8.6%-55.6%)	8.3 (6.2-12.5)	4.6 (2.3 - 13.5)
	TRALO 300mg	1,196	21.1%	10.8% (3.3%-30.3%)	2.9 (2.3-4.1)	14.7 (5.4 - 49.0)
	UPA 15mg	557	86.8%	38.7% (15.1%-68.9%)	15.5 (11.9-19.3)	2.9 (1.8 - 7.2)

Table S7. SUCRA, Response Rate, OR, and NNT for All Efficacy Outcomes at Week 8 (Bayesian NMA Fixed Effects Results) (continued)

Endpoint (continued)	Treatment (continued)	N[a]	SUCRA (continued)	Response Rate, Median (95% CI) (continued)	Odds Ratio vs Placebo, Median (95% CI) (continued)	NNT vs. Placebo, Median (95% CI) (continued)
	UPA 30mg	567	100.0%	51.1% (22.8%-78.7%)	25.7 (19.7-32.0)	2.1 (1.5 - 4.6)
	Placebo	2,214	0.0%	3.9% (1.2%-12.3%)	--	--
∆NRS≥4	ABRO 100mg	314	24.4%	24.8% (11.4%-46.2%)	3.8 (2.3-6.5)	6.1 (3.1-14.9)
	ABRO 200mg	309	68.5%	41.5% (21.8%-64.9%)	8.1 (4.9-14.0)	3.0 (2.0-5.8)
	BARI 2mg	392	23.4%	25.0% (11.9%-45.1%)	3.8 (2.5-5.9)	6.0 (3.3-13.4)
	BARI 4mg	248	51.4%	33.9% (17.1%-56.3%)	5.9 (3.7-9.4)	3.9 (2.4-7.9)
	DUP Q2W	457	48.6%	33.1% (17.2%-54.4%)	5.7 (3.9-8.3)	4.0 (2.5-7.8)
	TRALO 300mg		--	--	--	--
	UPA 15mg	557	83.8%	50.7% (30.5%-70.8%)	11.7 (8.5-16.5)	2.4 (1.8-3.8)
	UPA 30mg	567	100.0%	65.4% (44.6%-81.7%)	21.6 (15.5-30.5)	1.8 (1.5-2.5)
	Placebo	1,814	0.0%	8.0% (3.8%-16.1%)	--	--

[a] N represents sample size of trial arms used in the NMA
[b]Baseline-risk adjusted model was selected based on model fit statistics

ΔNRS≥4, Worst Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; ABRO, abrocitinib; BARI, baricitinib; CI, credible interval; DUPI, dupilumab; IGA, Investigator Global Assessment for Atopic Dermatitis; NMA, network meta-analysis; NNT, number needed to treat; SUCRA, surface under the cumulative ranking curve; UPA, upadacitinib.

Table S8. Number of responders for each outcome and ITT population for each trial used in the network meta-analysis

			Week 2				Week 4				Week 8				Primary Endpoint Timepoint			
Study	**Treatment**	**N**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**
JADE MONO-1	Abrocitinib 200mg	154	37[a]	8[a]	15[a]	67	72[a]	37[a]	41[a]	86	89[a]	51[a]	55[a]	88[a]	96	59	67	84
	Abrocitinib 100mg	156	16[a]	3[a]	6[a]	30	42[a]	12[a]	16[a]	47	59[a]	22[a]	31[a]	50[a]	62	29	37	55
	Placebo	77	3[a]	1[a]	0[a]	2	11[a]	3[a]	4[a]	13	10[a]	4[a]	5[a]	11[a]	9	4	6	11
JADE MONO-2	Abrocitinib 200mg	155	37[a]	14[a]	22[a]	54[a]	78[a]	35[a]	51[a]	77[a]	93[a]	53[a]	58[a]	79[a]	94	58[b]	59[b]	85[b]
	Abrocitinib 100mg	158	16[a]	4[a]	8[a]	36[a]	41[a]	15[a]	22[a]	49[a]	68[a]	27[a]	35[a]	61[a]	69	38[b]	44[b]	71[b]
	Placebo	78	1[a]	0[a]	0[a]	3[a]	5[a]	0[a]	1[a]	3[a]	10[a]	2[a]	8[a]	9[a]	8	3[b]	7[b]	9[b]
BREEZE-AD1	Baricitinib 4mg	125	17[c]	3[c]	6[c]	20[c]	29[c]	8[c]	13[c]	28[c]	34[c]	12[c]	16[c]	34[c]	31	20	21	23
	Baricitinib 2mg	123	8[c]	1[c]	3[c]	10[c]	16[c]	7[c]	11[c]	15[c]	21[c]	6[c]	11[c]	17[c]	23	13	14	12
	Placebo	249	3[c]	0[c]	5[c]	0[c]	6[c]	3[c]	6[c]	7[c]	13[c]	7[c]	6[c]	15[c]	22	12	12	16
BREEZE-AD2	Baricitinib 4mg	123	21[c]	5[c]	10[c]	13[c]	31[c]	16[c]	19[c]	23[c]	34[c]	12[c]	18[c]	26[c]	26	16	17	20
	Baricitinib 2mg	123	16[c]	4[c]	8[c]	8[c]	25[c]	10[c]	10[c]	14[c]	25[c]	14[c]	11[c]	22[c]	22	11	13	16
	Placebo	244	9[c]	3[c]	5[c]	2[c]	9[c]	5[c]	9[c]	5[c]	14[c]	7[c]	9[c]	14[c]	15	6	11	10
BREEZE-AD5	Baricitinib 2mg	146	25[c]	NR	11[c]	16[c]	35[c]	NR	12[c]	23[c]	37[c]	NR	18[c]	33[c]	43[b]	30[b]	35[b]	33[b]
	Placebo	147	7[c]	NR	3[c]	2[c]	13[c]	NR	4[c]	5[c]	12[c]	NR	6[c]	6[c]	12[b]	5[b]	8[b]	7[b]
SOLO 1	Dupilumab 300mg	224	NR	NR	NR	20	NR	NR	NR	34	NR	NR	NR	NR	115	80	85	87
	Placebo	224	NR	NR	NR	7	NR	NR	NR	13	NR	NR	NR	NR	33	17	23	26
SOLO 2	Dupilumab 300mg	233	NR	NR	NR	24	NR	NR	NR	51	NR	NR	NR	NR	103	70	84	81
	Placebo	236	NR	NR	NR	2	NR	NR	NR	14	NR	NR	NR	NR	28	17	20	21
SOLO 1 & 2 Pooled[d]	Dupilumab 300mg	457	48[b]	20[b]	17[b]	-	127[b]	47[b]	55[b]	-	205[b]	88[b]	106[b]	162[c]	-	-	-	-
	Placebo	460	15[b]	3[b]	2[b]	-	32[b]	8[b]	10[b]	-	45[b]	14[b]	12[b]	41[c]	-	-	-	-
ECZTRA 1	Tralokinumab 300mg	603	28[c]	3[c]	7	NR	73[c]	21[c]	24	NR	135[c]	51[c]	53	NR	150	87	95	119
	Placebo	199	9[c]	4[c]	4	NR	15[c]	4[c]	4	NR	25[c]	5[c]	9	NR	25	8	14	20

Table S8. Number of responders for each outcome and ITT population for each trial used in the network meta-analysis (continued)

			Week 2				Week 4				Week 8				Primary Endpoint Timepoint			
Study	**Treatment**	**N**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**	**EASI-75**	**EASI-90**	**IGA 0/1**	**ΔNRS≥4**
ECZTRA 2	Tralokinumab 300mg	593	28 [c]	8 [c]	7	NR	81 [c]	27 [c]	30	NR	155 [c]	61 [c]	70	NR	196	108	131	144
	Placebo	201	2 [c]	0 [c]	1	NR	6 [c]	0 [c]	1	NR	14 [c]	4 [c]	4	NR	23	11	22	19
MEASURE UP 1	Upadacitinib 30mg	285	135	59	60	135	214	135	135	187	228	170	160	201	227	187	177	168
	Upadacitinib 15mg	281	107	50	46	89	175	100	94	141	196	141	133	166	196	149	135	143
	Placebo	281	10	1	3	6	25	8	9	12	37	15	22	27	46	23	24	32
MEASURE UP 2	Upadacitinib 30mg	282	124	51	60	110	199	117	107	170	211	156	138	187	206	165	147 [b]	167
	Upadacitinib 15mg	276	91	38	37	81	151	76	79	132	178	97	91	136	166	117	107 [b]	113
	Placebo	278	10	2	1	6	14	5	3	10	28	7	7	25	37	15	13 [b]	25

[a] The number of responders was calculated using the population and the percentage as reported on clinicaltrials.gov.
[b] The number of responders was calculated using the population and the published percentage.
[c] The number of responders was calculated using the population and a digitized percentage.
[d] SOLO trials were used in place of SOLO 1 & 2 pooled data where available.
Note: The primary endpoint timepoint for each trial was week 12 for abrocitinib and week 16 for all other targeted therapies. All sources are cited in manuscript.
ΔNRS≥4, Pruritus Numerical Rating Scale reduction of ≥4 points from baseline; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment for Atopic Dermatitis; NR, not reported

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