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of bibliographic databases to identify published studies and 2) non-database search methods to identify in-process, unpublished, or grey literature [1].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 ABT494 or ABT494 or 4RA0KN46E0 or 1310726-60-3 or 1607431-21-9).ti,ab,kf,kw,ot,rm,nm. |
| 9. (Dupilumab* or dupixent* or regn 668 or REGN-668 or regn668 or sar 231893 or sar-231893 or sar231893 or 420K487FG or 1190264-60-8).ti,ab,kf,kw,ot,rm,nm. |
| 10. exp phototherapy/ |
| 11. (Phototherap* or light therap* or ultraviolet or ultra violet or broadband or broad band or narrow band or narrow band or UVB or PUVA or Psoralen or UVA or UVA1).ti,ab,kf,kw,ot,rm,nm. |
| 12. Azathioprine/ |
| 13. (Azathioprin* or arathioprin* or AZA or aza-q or azafalk* or azahexal* or azamedac* or azamun* or azarin* or azapin* or azapress* or azaprin* or azarex* or azasan* or azathiouric* or azathioprim* or azathioprinum* or azathiopurin* or azaspin* or azatil* or azatim* or azatil* or azathiope* or colinsan* or immuran* or immurel* or immuthera* or imunen* or imuprin* or imuran* or imurek* or imuren* or muran* or murasul* or thioazeprin* or thiazepin* or thioprin* or transimun* or szym* or A13-50290 or bw 57 322 or bw-57322 or bw57322 or bw-57-322 or bw57322 or CCRIS 62 or CCRIS-62 or CCRIS62 or cccul* 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,rm,nm. |
| 14. Ciclosporin/ |
| 15. (Ciclosporin* or abrammun* or aqua-stasis* or aquastasis* or arpinum* or cequa* or ciclomulsion* or cicaloral* or ciclospirina* or ciclospirine* or ciclosporinum* or cipol* or consupren* or cyclasol* or cyclo-derm* or cyclokat* or cyclosporin* or dexamune* or equoral* or gengraf* or hydro-stasis* or ikervis* or iminoral* or implant* or imusporin* or neoplasia* or neoral-sandimmun* or neoral* or neural* or neuro-stat* or neurostat* or oplisporin* or optimun* or padcielo* or papillock* or pulminiq* or "Ramihyphin A" or restasis* or restayis* or sanciclo* or sandimmun* or sandimun* or sangcy* or vekacia* or verkasia* or "27400" or "de 076" or "DRG 0275" or "nm 0133" or "opph 088" or "stib 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 nova22007 or nsc 290193 or nsc-290193 or NSC290193 or ol 27400 or ol-27-400 or ol27400 or olo 400 or olo 400 or olo 400 or olo 400 or opph-088 or opph088 or opph 088 or otx 101 or
tox-101 or tox101 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
nm133 or
nm0133 or nova 22007 or
nova22007 or nova-22007 or nova22007 or NSC 290193 or NSC-290193 or NSC290193 or ol 27400 or ol-27-400 or
ol-27400 or ol 400 or olo 400 or olo-400 or olo-500 or olo 500 or opph-088 or opph088 or opph 088 or otx 101 or
otx-101 or tox101 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 sti-0529 or t1580 or t-1580 or t1580 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 arexel*
or
bendatrexat* or biotrexa or trimexat* or canceren* or carditrex* or dermotrex* or ebetrex* or entrexat* or
emthexat* or
emthexat* or entrexat* or enthexat* or farmitlexat* or farmotrex* 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
metatrexat* or methylaminopterin* or methylfolic acid or methylpteroylglutamic acid or
metrical* or
metoject* or metothrexat* or metotrextato* or metotrexino* or metrex* or mexit-or
mtex* 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 xatmepl* or xetazat* or "EINECS 200-413-8" or 31G1E710ZN or AI325299 or
AI-325299 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
YL5F22YSU1 or 15475-56-6 or
99-05-2 or 7413-34-5).ti,ab,kf,kw,ot,rn,nm.
18 Alitretinoin/
19 (Alitretinoin* or alitretinoinum* or cehado* or hanzema* or panretin* or pan.retyn* or panrexin*
or
retinoic acid*
or
toctino* or tretinoin* or agn 192013 or agn-192013 or agn192013 or alt 1057 or alt-1057 or alt1057 or alt 1057 or
alt1057 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
1U8E65K8DZ or 5300-03-8).ti,ab,kf,kw,ot,rn,nm.
20 Mycophenolate Mofetil/
21 (mycophenalat* or mofetil* or MMF or cell cept* or cellcept* or cellmum* 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
9242EC6W6R0 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 oliman* 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 ISP444213Y or 1187594-09-7).ti,ab,kf,kw,ot,nn,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,nn,nm.
25 Prednisolone/
26 (Prednisolone or Adelcort* or Ak-Pred* or Antisolon* or Apredislon* or Benisolon* or Berisolon* or Bubbli-Pred* or Calberdelt* or Cambison* or Capsoid* or "co hydrelta"* or Codelcorton* or Compresolon* or Cordrol* or Cortadelton* or Cortalon* or Cortelinter* or Cortisolon* or Cotogesic* or Cotolon* or Decaptin* 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 cortisol* or "delta f" or "delta hycortol"* or "delta hydrocortisone"* or "delta opticor"* or "delta stab" or delta-hydrocortison* or "delta1 dehydrocortisol"* or "delta1 dehydrocortison"* or Deltacortef* or Deltacortenol* or Deltacortenolo* or Deltacortil* or Deltaderm* or Deltaglycortril* or Deltahycortol* or Deltahydrocortison* or Deltaopthicor* or Deltasolomon* or Deltason* or Deltastab* or Deltidrosol* or Deltisilon* or Deltisolon* or Deltolasson* or Deltolasson* or Deltaison* or Depopredat* or Depo predat* or Dermosolon* or "Derpo PD" or Dhasolon* 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 Erbacton* or Erbason* or Estilson* or Fernisolon* or Glistelon* or Hefasolon* or Hostacortin* or Hydrelta* or Hydreltrasol* or Hydeltron* or Hydrocortan* or Hydrocortide* or Hydrodeltalon* or Hydrodeltison* or Hydroretrocortin* or Inflamas* or Infinityefran* or Insolon* or Keteocort* or Key pred* or Klismacort* or Lenisolon* or Lentoison* or Leocortol* or Liquipred* or "liquid pred" or lygal koptfinktur or mediasolon* or meprisolon* or meprisolon* 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 Panacortelon* or Panafort* or Paracortol* or Paracotol* or Pediapred* or Phlogex* or Poly-Pred* or PRDL or pre cortisol* or preconin* or precortalon* or Precortancyl* or Precortilon* or Precortisyl* or Pred ject* or Predject* or Predacort* or Predalon* or Predartin* or Predat* or Predeltilon* or Predisol* or Predisyr* or predhe dom* or prednecort* or prednedom* or prednelan* or predni coelin* or predni h tablinen* or predni-helvacort* or Prednicen* or Prednicocelin* or Prednicort* or Prednicortelon* or prednifor drops* or Predniliderm* or Predniment* or Predniretard* or Prednis* or Prednisil* or Prednisolone* or prednisolon* or Prednisolonom* or Prednivet* or Prednorsolon* or Predonor* or Predonin* or Predorgasolon* or Predorga solon* or Preflam* or Prelon* or Premilon* or Prelin* or Prenin* or Preolon* 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 Spoloten* 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
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 |
| **Comparators**   | • Placebo • Active intervention (i.e., head-to-head trials)                          | Studies containing: • Use of concomitant TCS or TCI therapies |
| **Outcomes**      | Efficacy • EASI • IGA • PRO • Pruritus NRS‡                                         | Studies only containing: • TCS • Systemic immunosuppressants • Topical retinoids • Phototherapy • Prednisolone |
| **Study design**  | • Randomized controlled trials (phase III, IV) • Randomized crossover/cluster trials, provided randomized phase is at least 12 weeks | Studies only containing: • 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; DLOI, 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    | Yes         | Yes         | Yes       | Yes          | Yes          |
| JADE MONO-2    | Yes         | Yes         | Yes       | Yes          | Yes          |
| BREEZE-AD 1    | Yes         | Yes         | Yes       | Yes          | Yes          |
| BREEZE-AD 2    | Yes         | Yes         | Yes       | Yes          | Yes          |
| BREEZE-AD 5    | Yes         | Yes         | Yes       | Yes          | Yes          |
| SOLO 1         | Yes         | Yes         | Yes       | Yes          | Yes          |
| SOLO 2         | Yes         | Yes         | Yes       | Yes          | Yes          |
| ECZTRA 1       | Yes         | Yes         | Yes       | Yes          | Yes          |
| ECZTRA 2       | Yes         | Yes         | Yes       | Yes          | Yes          |
| Measure Up 1   | Yes         | Yes         | Yes       | Yes          | Yes          |
| Measure Up 2   | Yes         | Yes         | Yes       | Yes          | Yes          |

1. Was randomization carried out appropriately?
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes
   - Yes

2. 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
   - 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 dropouts between groups? If so, were they explained or adjusted for?
   - No
   - Yes
   - Yes
   - No
   - Yes
   - No
   - Yes
   - No
   - No
   - Yes
   - No
   - Yes
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 | 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 | 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 | 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.

$\Delta NRS \geq 4$, Pruritus Numerical Rating Scale reduction of $\geq 4$ 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

| Treatment | Upadacitinib 30 mg | Upadacitinib 15 mg | Abrocitinib 100 mg | Abrocitinib 30 mg | Dupilumab 300 mg | Placebo |
|-----------|--------------------|--------------------|--------------------|------------------|-----------------|---------|
| **Plasma** |                   |                    |                    |                  |                 |         |
| **16.47** | **11.50**          | **7.77**           | **3.31**           | **0.28**         | **2.56**        | **2.24** |
| (12.37, 20.70) | (7.77, 18.45) | (3.31, 6.49) | (0.28, 3.20) | (2.56, 7.47) | (2.24, 7.38) | (1.87, 6.22) |
| **16.75** | **12.90**          | **9.61**           | **5.27**           | **2.37**         | **3.49**        | **2.09** |
| (4.60, 18.55) | (9.61, 28.21) | (5.27, 10.64) | (2.37, 4.68) | (3.49, 8.34) | (2.09, 3.87) | (0.89, 5.80) |
| **Baricitinib 1 mg** | **18.67** | **16.82** | **10.37** | **6.35** | **11.82** | **7.02** |
| (3.18, 10.48) | (16.82, 50.36) | (10.37, 21.77) | (6.35, 11.24) | (11.82, 33.65) | (7.02, 29.61) | (1.83, 7.02) |
| **Abrocitinib 100 mg** | **18.67** | **16.82** | **10.37** | **6.35** | **11.82** | **7.02** |
| (3.18, 10.48) | (16.82, 50.36) | (10.37, 21.77) | (6.35, 11.24) | (11.82, 33.65) | (7.02, 29.61) | (1.83, 7.02) |
| **Baricitinib 1 mg** | **18.67** | **16.82** | **10.37** | **6.35** | **11.82** | **7.02** |
| (3.18, 10.48) | (16.82, 50.36) | (10.37, 21.77) | (6.35, 11.24) | (11.82, 33.65) | (7.02, 29.61) | (1.83, 7.02) |

### EASI-75

| Treatment | Upadacitinib 30 mg | Upadacitinib 15 mg | Abrocitinib 100 mg | Abrocitinib 30 mg | Dupilumab 300 mg | Placebo |
|-----------|--------------------|--------------------|--------------------|------------------|-----------------|---------|
| **Plasma** |                   |                    |                    |                  |                 |         |
| **11.99** | **9.60**           | **7.50**           | **4.88**           | **1.00**         | **1.00**        | **1.00** |
| (7.85, 18.09) | (5.26, 16.48) | (4.88, 7.50) | (1.00, 7.50) | (1.00, 1.00) | (1.00, 1.00) | (1.00, 1.00) |
| **11.99** | **9.60**           | **7.50**           | **4.88**           | **1.00**         | **1.00**        | **1.00** |
| (7.85, 18.09) | (5.26, 16.48) | (4.88, 7.50) | (1.00, 7.50) | (1.00, 1.00) | (1.00, 1.00) | (1.00, 1.00) |
| **Baricitinib 1 mg** | **11.99** | **9.60** | **7.50** | **4.88** | **1.00** | **1.00** |
| (7.85, 18.09) | (5.26, 16.48) | (4.88, 7.50) | (1.00, 7.50) | (1.00, 1.00) | (1.00, 1.00) | (1.00, 1.00) |
| **Abrocitinib 100 mg** | **11.99** | **9.60** | **7.50** | **4.88** | **1.00** | **1.00** |
| (7.85, 18.09) | (5.26, 16.48) | (4.88, 7.50) | (1.00, 7.50) | (1.00, 1.00) | (1.00, 1.00) | (1.00, 1.00) |
| **Baricitinib 1 mg** | **11.99** | **9.60** | **7.50** | **4.88** | **1.00** | **1.00** |
| (7.85, 18.09) | (5.26, 16.48) | (4.88, 7.50) | (1.00, 7.50) | (1.00, 1.00) | (1.00, 1.00) | (1.00, 1.00) |

### EASI-90

| Treatment | Upadacitinib 30 mg | Upadacitinib 15 mg | Abrocitinib 100 mg | Abrocitinib 30 mg | Dupilumab 300 mg | Placebo |
|-----------|--------------------|--------------------|--------------------|------------------|-----------------|---------|
| **Plasma** |                   |                    |                    |                  |                 |         |
| **14.27** | **13.04**          | **8.50**           | **5.27**           | **2.37**         | **3.49**        | **2.09** |
| (10.77, 18.09) | (8.50, 26.27) | (5.27, 10.64) | (2.37, 4.68) | (3.49, 8.34) | (2.09, 3.87) | (0.89, 5.80) |
| **14.27** | **13.04**          | **8.50**           | **5.27**           | **2.37**         | **3.49**        | **2.09** |
| (10.77, 18.09) | (8.50, 26.27) | (5.27, 10.64) | (2.37, 4.68) | (3.49, 8.34) | (2.09, 3.87) | (0.89, 5.80) |
| **Baricitinib 1 mg** | **14.27** | **13.04** | **8.50** | **5.27** | **2.37** | **2.09** |
| (10.77, 18.09) | (8.50, 26.27) | (5.27, 10.64) | (2.37, 4.68) | (3.49, 8.34) | (2.09, 3.87) | (0.89, 5.80) |
| **Abrocitinib 100 mg** | **14.27** | **13.04** | **8.50** | **5.27** | **2.37** | **2.09** |
| (10.77, 18.09) | (8.50, 26.27) | (5.27, 10.64) | (2.37, 4.68) | (3.49, 8.34) | (2.09, 3.87) | (0.89, 5.80) |
| **Baricitinib 1 mg** | **14.27** | **13.04** | **8.50** | **5.27** | **2.37** | **2.09** |
| (10.77, 18.09) | (8.50, 26.27) | (5.27, 10.64) | (2.37, 4.68) | (3.49, 8.34) | (2.09, 3.87) | (0.89, 5.80) |
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

| Treatment | Placebo | Upadacitinib 30 mg | Upadacitinib 15 mg | Abrocitinib 200 mg | Abrocitinib 10 mg | Danlucinam 30 mg | Danlucinam 20 mg | Abrocitinib 80 mg | Abrocitinib 40 mg | Placide | p-value |
|-----------|---------|-------------------|-------------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|---------|---------|
| EASI-75   |         |                   |                   |                  |                 |                 |                 |                 |                 |         |         |
| Delta NRS≥4 | 0.59    | 0.37              | 0.24              | 0.17             | 0.12            | 0.08            | 0.05            | 0.04            | 0.02            | 0.01    | 0.00    |

#### ΔNRS≥4

| Treatment | Placebo | Upadacitinib 30 mg | Upadacitinib 15 mg | Abrocitinib 200 mg | Abrocitinib 10 mg | Danlucinam 30 mg | Danlucinam 20 mg | Abrocitinib 80 mg | Abrocitinib 40 mg | Placide | p-value |
|-----------|---------|-------------------|-------------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|---------|---------|
| ΔNRS≥4    | 0.59    | 0.37              | 0.24              | 0.17             | 0.12            | 0.08            | 0.05            | 0.04            | 0.02            | 0.01    | 0.00    |

* Asterisks indicate significance (odds ratio credible intervals do not cross 1).
### Table S5. Overview of results for the network meta-analysis 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 pooleda   | Dupilumab 300mg    | 457 | 10.5%   |        |
|                | Placebo            | 460 | 3.3%    |        |
| ECZTRA 1b      | Tralokinumab 300mg | 603 | 4.7%    |        |
|                | Placebo            | 199 | 4.5%    |        |
| ECZTRA 2b      | 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%   |

Data from SOLO 1 and SOLO 2 were pooled for analysis for EASI-75 as reported in Thaci et al., 2019 [9]

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.

$\Delta \text{NRS} \geq 4$, Pruritus Numerical Rating Scale reduction of $\geq 4$ 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)

**EASI-75**

- UPA 30 mg
- ABRO 200 mg
- UPA 15 mg
- DUP Q2W
- ABRO 100 mg
- BARI 4 mg
- BARI 2 mg
- TRALO 300 mg
- Placebo

**EASI-90**

- UPA 30 mg
- ABRO 200 mg
- UPA 15 mg
- DUP Q2W
- ABRO 100 mg
- BARI 4 mg
- BARI 2 mg
- TRALO 300 mg
- Placebo
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; DUP, 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  | SUCRA | Response Rate, Median (95% CI) | Odds Ratio vs Placebo, Median (95% CI) | NNT vs. Placebo, Median (95% CI) |
|----------|---------------|----|-------|------------------------------|----------------------------------------|----------------------------------|
| EASI-75b | 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<sup>a</sup> | 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%)  | —                               | —                               | —                               |
| ΔNRS≥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%)               | —                               | —                               |

<sup>a</sup> N represents sample size of trial arms used in the NMA

<sup>b</sup> 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 | 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| 8.6%  | 13.2% (5.0%-32.9%) | 4.8 (2.1-12.7) | 10.0 (3.5-35.7) |
|            | 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 0/1b   | 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<sup>a</sup> | 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%)                           | --                                               | --                                            |

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

∆NRS≥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

| 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 | EASI-75 | EASI-90 | IGA 0/1 | ΔNRS≥4 |
|-------------|------------|----|---------|---------|---------|--------|---------|---------|---------|--------|---------|---------|---------|--------|---------|---------|---------|--------|---------|---------|---------|--------|
| JADE MONO-1 | Abrocitinib 200mg | 154 | 37 | 8 | 15 | 67 | 72 | 37 | 41 | 86 | 89 | 51 | 55 | 88 | 96 | 59 | 67 | 84 | 156 | 16 | 3 | 6 | 30 | 42 | 12 | 16 | 47 | 59 | 22 | 31 | 50 | 62 | 29 | 37 | 55 |
|             | Abrocitinib 100mg | 156 | 16 | 3 | 6 | 30 | 42 | 12 | 16 | 47 | 59 | 22 | 31 | 50 | 62 | 29 | 37 | 55 | 77 | 37 | 14 | 22 | 54 | 78 | 35 | 51 | 77 | 93 | 53 | 58 | 79 | 94 | 58 | 59 | 85 |
|             | Placebo     | 77  | 3  | 1  | 0  | 2  | 11 | 3  | 4  | 13 | 10 | 4  | 5  | 11 | 9  | 4  | 6  | 11 | 155 | 37 | 14 | 22 | 54 | 78 | 35 | 51 | 77 | 93 | 53 | 58 | 79 | 94 | 58 | 59 | 85 |
| JADE MONO-2 | Abrocitinib 200mg | 158 | 16 | 4 | 8 | 36 | 41 | 15 | 22 | 49 | 68 | 27 | 35 | 61 | 69 | 38 | 44 | 71 | 125 | 17 | 3 | 6 | 20 | 29 | 8 | 13 | 28 | 34 | 12 | 16 | 34 | 31 | 20 | 21 | 23 |
|             | Abrocitinib 100mg | 158 | 16 | 4 | 8 | 36 | 41 | 15 | 22 | 49 | 68 | 27 | 35 | 61 | 69 | 38 | 44 | 71 | 78  | 1  | 0 | 0 | 3 | 5 | 0 | 1 | 3 | 10 | 2 | 8 | 9 | 8 | 3 | 7 | 9 |
|             | Placebo     | 78  | 1  | 0 | 0 | 3 | 5 | 0 | 1 | 3 | 10 | 2 | 8 | 9 | 8 | 3 | 7 | 9 | 125 | 17 | 3 | 6 | 20 | 29 | 8 | 13 | 28 | 34 | 12 | 16 | 34 | 31 | 20 | 21 | 23 |
| BREEZE-AD1  | Baricitinib 4mg | 123 | 8 | 1 | 3 | 10 | 16 | 7 | 11 | 15 | 21 | 6 | 11 | 17 | 23 | 13 | 14 | 12 | 123 | 16 | 4 | 8 | 8 | 25 | 10 | 10 | 14 | 25 | 14 | 11 | 22 | 22 | 11 | 13 | 16 |
|             | Baricitinib 2mg | 249 | 3 | 0 | 5 | 0 | 6 | 3 | 6 | 7 | 13 | 7 | 6 | 15 | 22 | 12 | 12 | 16 | 244 | 9 | 3 | 5 | 2 | 9 | 5 | 9 | 5 | 14 | 7 | 9 | 14 | 15 | 6 | 11 | 10 |
|             | Placebo     | 123 | 21 | 5 | 10 | 13 | 31 | 16 | 19 | 23 | 34 | 12 | 18 | 26 | 26 | 16 | 17 | 20 | 146 | 25 | 11 | 16 | 35 | 35 | 12 | 23 | 37 | 18 | 33 | 33 | 43 | 30 | 35 | 33 |
| BREEZE-AD2  | Baricitinib 4mg | 123 | 16 | 4 | 8 | 8 | 25 | 10 | 10 | 14 | 25 | 14 | 11 | 22 | 22 | 11 | 13 | 16 | 146 | 25 | 11 | 16 | 35 | 35 | 12 | 23 | 37 | 18 | 33 | 33 | 43 | 30 | 35 | 33 |
|             | Baricitinib 2mg | 244 | 9 | 3 | 5 | 2 | 9 | 5 | 9 | 5 | 14 | 7 | 9 | 14 | 15 | 6 | 11 | 10 | 244 | 9 | 3 | 5 | 2 | 9 | 5 | 9 | 5 | 14 | 7 | 9 | 14 | 15 | 6 | 11 | 10 |
|             | Placebo     | 147 | 7 | 3 | 2 | 13 | 4 | 5 | 12 | 6 | 6 | 12 | 5 | 8 | 7 | 12 | 5 | 8 | 7 | 224 | NR | NR | NR | 20 | NR | NR | NR | 34 | NR | NR | NR | 115 | 80 | 85 | 87 |
| BREEZE-AD5  | Placebo     | 224 | NR | NR | NR | 7 | NR | NR | NR | 13 | NR | NR | NR | 33 | 17 | 23 | 26 | 224 | NR | NR | NR | 7 | NR | NR | NR | 13 | NR | NR | NR | 33 | 17 | 23 | 26 |
| SOLO 1      | Dupilumab 300mg | 233 | NR | NR | NR | 24 | NR | NR | NR | 51 | NR | NR | NR | 103 | 70 | 84 | 81 | 233 | NR | NR | NR | 24 | NR | NR | NR | 51 | NR | NR | NR | 103 | 70 | 84 | 81 |
| SOLO 2      | Placebo     | 236 | NR | NR | NR | 24 | NR | NR | NR | 51 | NR | NR | NR | 103 | 70 | 84 | 81 | 236 | NR | NR | NR | 24 | NR | NR | NR | 51 | NR | NR | NR | 103 | 70 | 84 | 81 |
| SOLO 1 & 2 Pooled | Placebo     | 460 | 15 | 3 | 2 | 32 | 8 | 10 | 45 | 14 | 12 | 41 | c | - | - | - | 460 | 15 | 3 | 2 | 32 | 8 | 10 | 45 | 14 | 12 | 41 | c | - | - | - |
| ECZTRA 1    | Placebo     | 603 | 28 | 3 | 7 | NR | 73 | 21 | 24 | NR | 135 | 51 | 53 | NR | 150 | 87 | 95 | 119 | 199 | 9 | 4 | 4 | NR | 15 | 4 | 4 | NR | 25 | 5 | 9 | NR | 25 | 8 | 14 | 20 | 29
Table S8. Number of responders for each outcome and ITT population for each trial used in the network meta-analysis (continued)

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

<sup>a</sup> The number of responders was calculated using the population and the percentage as reported on clinicaltrials.gov.

<sup>b</sup> The number of responders was calculated using the population and the published percentage.

<sup>c</sup> The number of responders was calculated using the population and a digitized percentage.

<sup>d</sup> 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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