Journal Club

Abrocitinib versus Placebo or Dupilumab for Atopic Dermatitis

2021.9.23

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Question

是否同意Abrocitinib長期使用在
中度至重度的異位性皮膚炎患者？

同意

需要更多
文獻支持

不同意

Outline

- Background
- Clinical trial
- Discussion
- Appraisal

Background

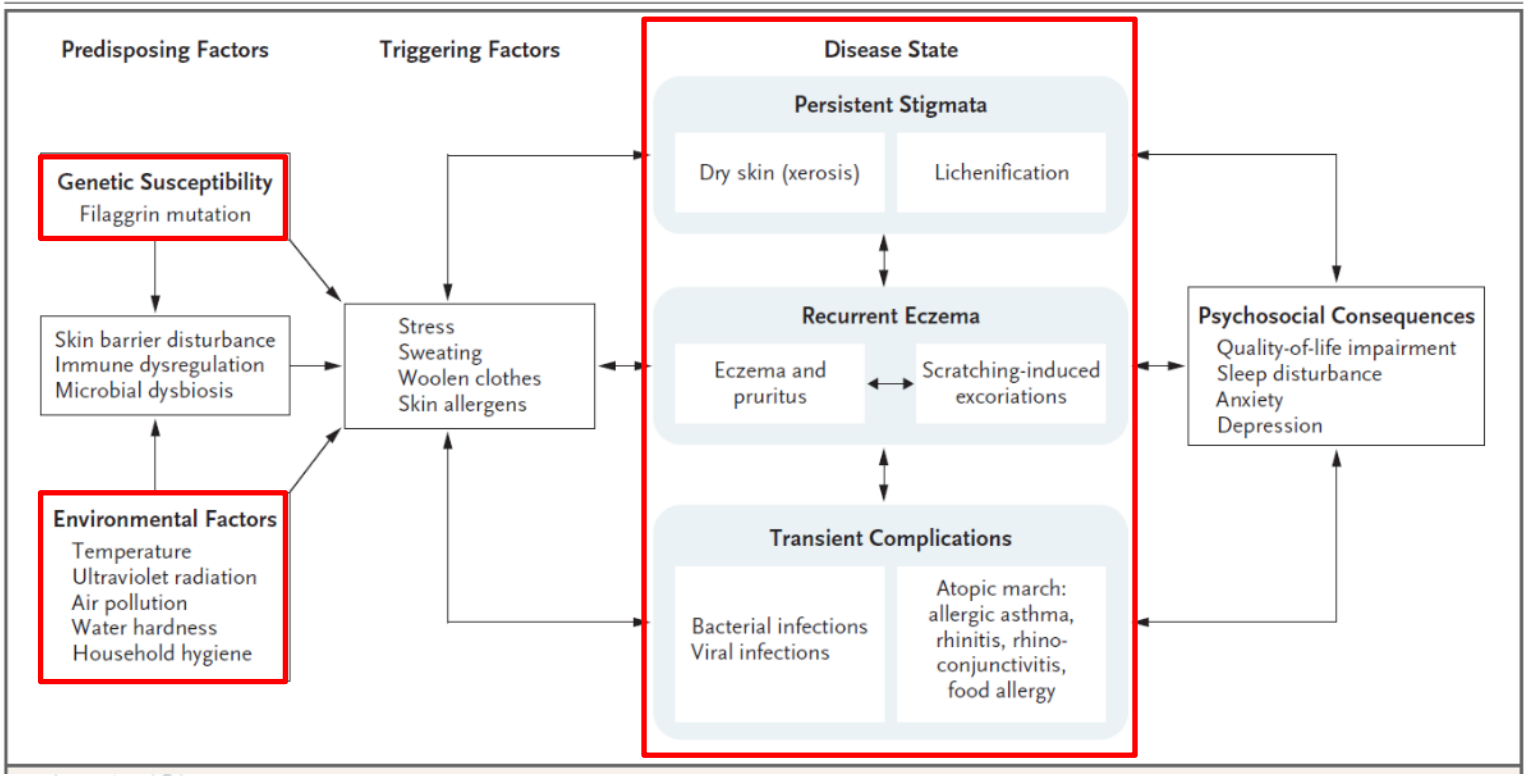
Atopic Dermatitis (AD)

Atopic Dermatitis

- **A chronic inflammatory skin disorder**
- Prevalence in Taiwan has increased significantly in the past few decades, ranging from 4.1% to 6.7% among selected cohorts.
- Usually develops in childhood and may persist into adulthood ;

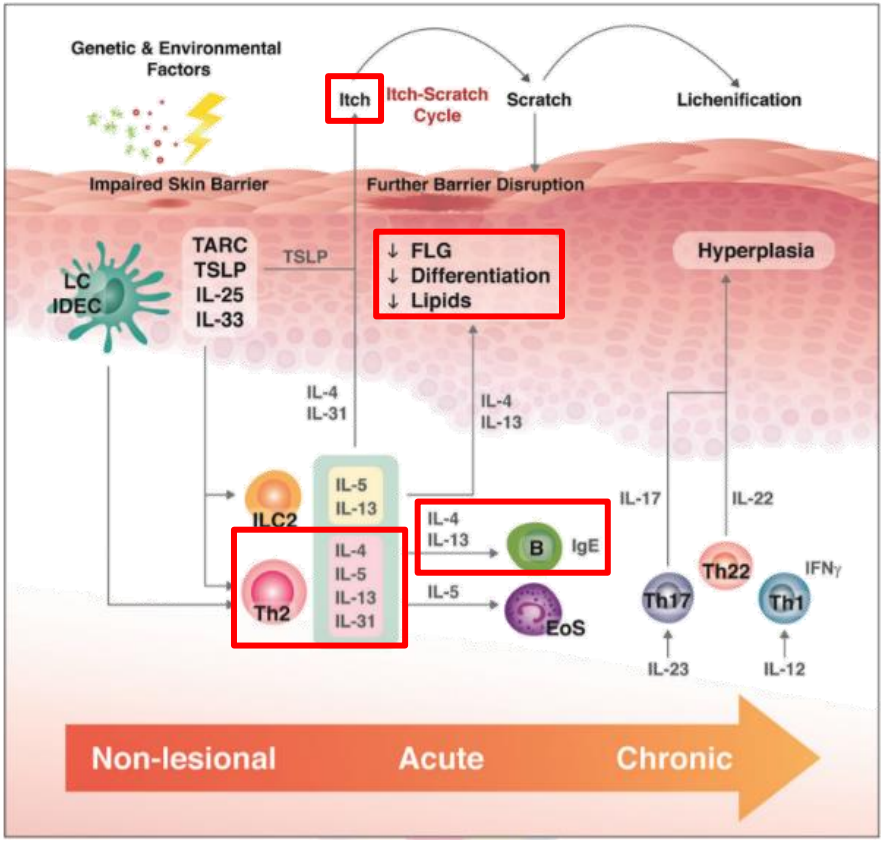
  less frequently, it starts in midlife or late life.
- Often associated with elevated serum **IgE** levels and a personal or family history of **type I allergies, allergic rhinitis, asthma and food allergies.**
- **Atopic eczema** is synonymous

Atopic Dermatitis



N Engl J Med 2021;384:1136-43. DOI: 10.1056/NEJMra2023911

Atopic Dermatitis – Pathogenesis



Cho YT, Chu CY. Advances in systemic treatment for adults with moderate-to-severe atopic dermatitis. Dermatol Sin 2019;37:3-11

Atopic Dermatitis – Treatment

1

- **Emollients**
- Topical corticosteroids
- Antihistamines
- Therapeutic patient education

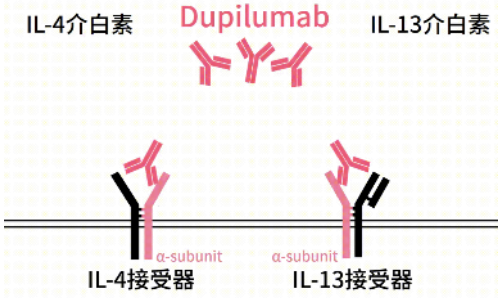
2

- Topical calcineurin inhibitors (鈣調磷酸酶抑制劑)
  - Tacrolimus (Protopic 0.1% Ointment®)
- Systemic corticosteroids (short-term therapy for acute flares)
- Topical and systemic antibiotics
- Phototherapy

3

- **Systemic immunomodulatory agents**
  - ○ Cyclosporine
  - ○ Azathioprine
  - ○ Methotrexate
  - ○ Mycophenolate mofetil
  - ● **Dupilumab**
  - ● **(Abrocitinib)**
- Antiseptics
- Complementary & alternative medicine

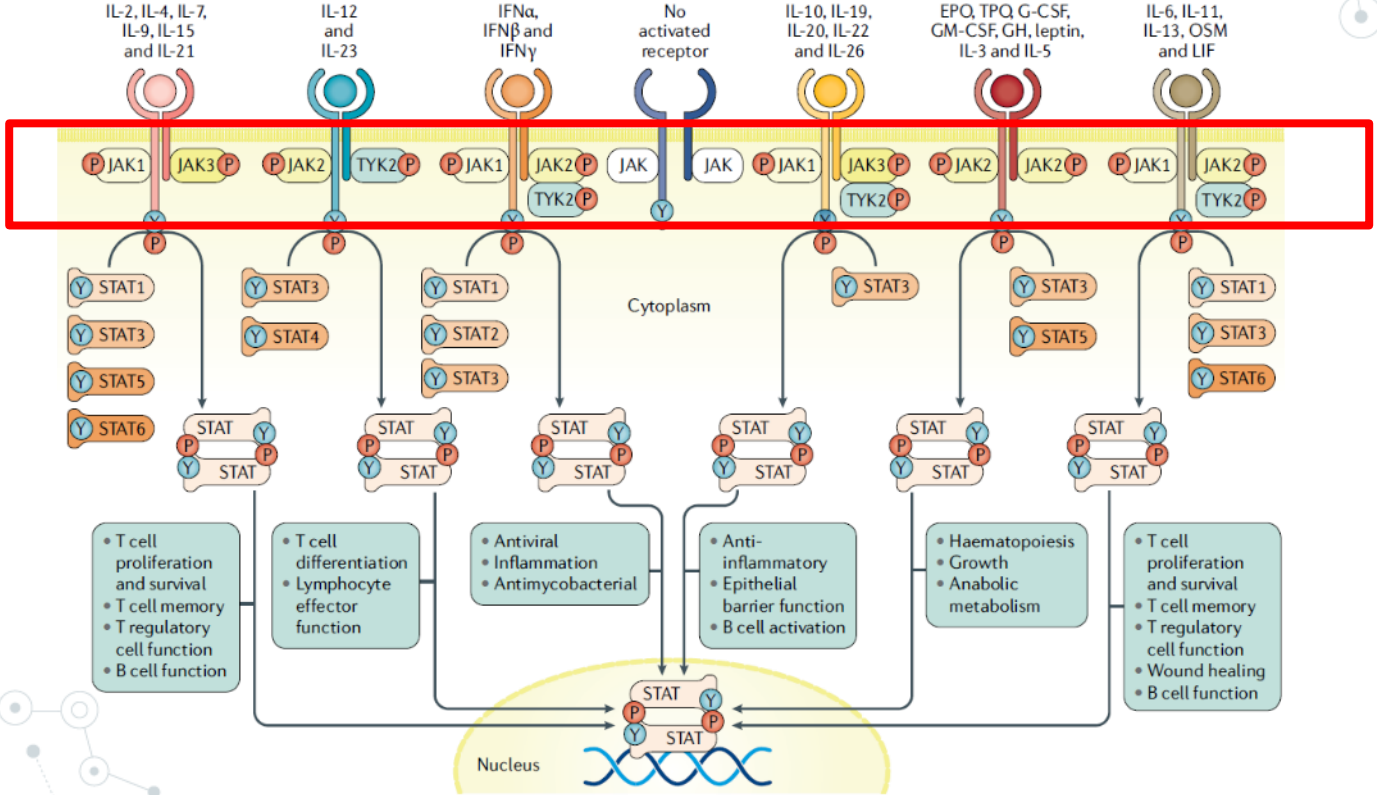
Atopic Dermatitis – Treatment



Dupilumab （Dupixent® 杜避炎注射劑）

- **Anti–IL-4–receptor α monoclonal antibody**
- **Inhibits IL-4, IL-13** signaling
- **Subcutaneous injection**
- Initial 600 mg loading dose followed by 300 mg injections every other week.
- Store refrigerated at **2°C to 8°C**
- Has been approved for adults with moderate-to-severe AD in Taiwan in May 2018.
- $ 19738 / syri

Atopic Dermatitis – Janus kinase (JAK) inhibitor



Nature Reviews Gastroenterology & Hepatology volume 17, pages323–337 (2020)

Atopic Dermatitis – Janus kinase (JAK) inhibitor

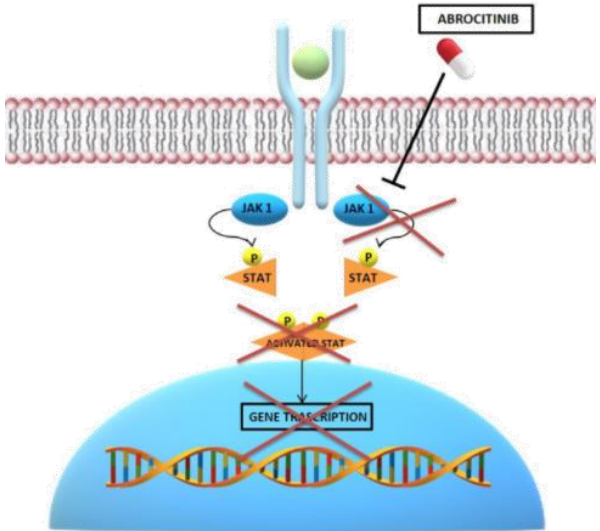
Abrocitinib

- a small-molecule **JAK1 inhibitor**
- Oral once daily

Tofacitinib（Xeljanz ® 捷抑炎）

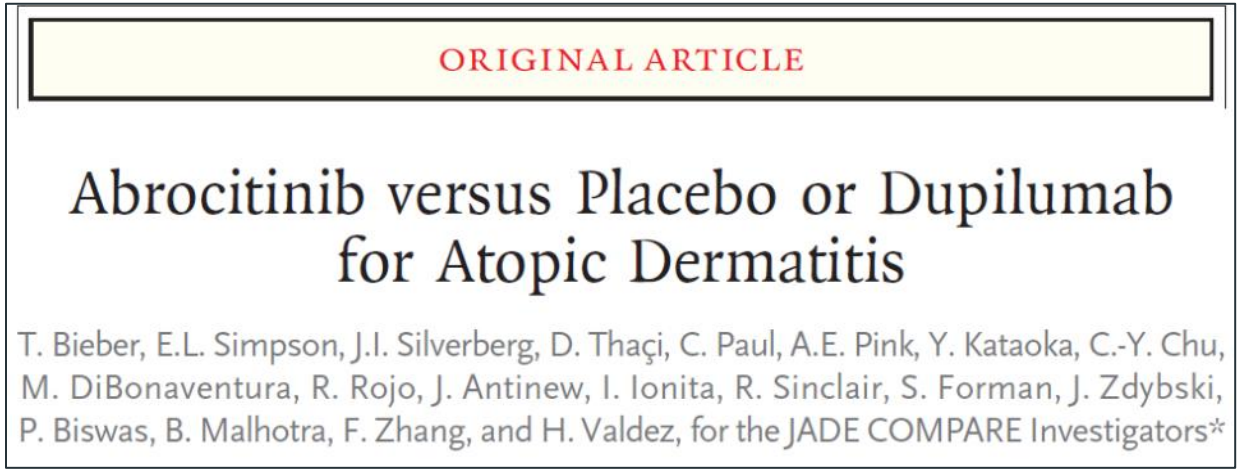
Baricitinib（Olumiant ® 愛滅炎）

Upadacitinib



The Efficacy and Safety of Abrocitinib as a Treatment Option for Atopic Dermatitis: A Short Report of the Clinical Data. Drug Des Devel Ther. 2021;15:1135-1147

Clinical trial



ORIGINAL ARTICLE

Abrocitinib versus Placebo or Dupilumab for Atopic Dermatitis

T. Bieber, E.L. Simpson, J.I. Silverberg, D. Thaçi, C. Paul, A.E. Pink, Y. Kataoka, C.-Y. Chu, M. DiBonaventura, R. Rojo, J. Antinew, I. Ionita, R. Sinclair, S. Forman, J. Zdybski, P. Biswas, B. Malhotra, F. Zhang, and H. Valdez, for the JADE COMPARE Investigators*

N Engl J Med 2021;384:1101-12.
DOI: 10.1056/NEJMoa2019380
March 25, 2021

Study Objective & Design

Study objective

P patient	Adults with moderate-to-severe atopic dermatitis who were receiving background topical therapy
I intervention	Abrocitinib 100mg or 200mg
C comparison	Dupilumab or Placebo
O outcome	efficacy and safety

Study design

A multicenter, randomized, double-blind, double-dummy, placebo-controlled trial

Patients
Investigators
Representatives of the sponsor

Patients – Inclusion criteria

1) 18 years of age or older
2) At least a 1-year history of AD that was **moderate to severe.**
   - ✓ BSA ≥ 10%
   - ✓ IGA ≥ 3
   - ✓ EASI ≥ 16
   - ✓ PP-NRS ≥ 4

Patients – Inclusion criteria

1) 18 years of age or older
2) At least a 1-year histo
   - ✓ BSA ≥ 10%
   - ✓ **IGA ≥ 3**
   - ✓ EASI ≥ 16
   - ✓ PP-NRS ≥ 4

Investigator's Global Assessment
研究者總體評估

Score	Morphological Description
0 – Clear	No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
1 – Almost clear	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
2 – Mild	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
3 – Moderate	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
4 – Severe	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.

Patients – Inclusion criteria

1) 18 years of age or older
2) At least a 1-year history of AD t
   - ✓ BSA ≥ 10%
   - ✓ IGA ≥ 3
   - ✓ **EASI ≥ 16**
   - ✓ PP-NRS ≥ 4

Eczema Area and Severity Index
濕疹面積與嚴重度指數

異位性皮膚炎面積（Area）：合併總面積估體表%_____

涵蓋程度	0%	1-9%	10-29%	30-49%	50-69%	70-89%	90-100%
面積分數	0	1	2	3	4	5	6

部位：頭部(h)、軀幹(t)、上肢(u)、下肢(l)

異位性皮膚炎嚴重度（Severity）：

嚴重度	None 無	Mild 輕度	Moderate 中度	Severe 重度
分數	0	1	2	3

異位性皮膚炎面積暨嚴重程度指數(EASI)評分表：

身體部位	Redness/ Erythema 發紅 (0-3)	Edema/ Papulation 浮腫/丘疹 (0-3)	Scratching/ Excoriation 抓痕 (0-3)	Lichenification 苔癬化 (0-3)	Region score 面積分數 (0-6)	Multiplier 乘數	身體部位分數
Head/neck 頭/ 頸	(+	+	+	)×		× 0.1	
Trunk 軀幹	(+	+	+	)×		× 0.3	
Upper limbs 上肢	(+	+	+	)×		× 0.2	
Lower limbs 下肢	(+	+	+	)×		× 0.4	
EASI 總分由四項身體部位分數加總							(0-72)

EASI = 0.1 (Red+Edema+Scratch+Lichenification)×(頭部%)+0.2 (Red+Edema+Scratch + Lichenification)×(上肢%) + 0.3 (Red + Edema + Scratch + Lichenification)×(軀幹%)+0.4(Red+Edema+Scratch+Lichenification)×(下肢%)

附註：Eczema area severity index (EASI)之異位性皮膚炎面積計算，只含皮膚紅腫濕疹部位，單純的皮膚乾燥、脫皮、抓痕，不可列入計算。

Patients – Inclusion criteria

1) 18 years of age or older
2) At least a 1-year history of AD that was **moderate to severe**
   - ✓ BSA ≥ 10%
   - ✓ IGA ≥ 3
   - ✓ EASI ≥ 16
   - ✓ **PP-NRS ≥ 4**

Peak Pruritus Numerical Rating Scale
搔癢數字等級量表
score 0-10

Patients – Inclusion criteria

3) An **inadequate response to topical medications** or a need for systemic therapy to control their disease during the 6 months before screening.

4) **Avoid pregnancy**

5) **Avoid** prolonged exposure to the sun, tanning booths, sun lamps or other **ultraviolet light** sources during the study

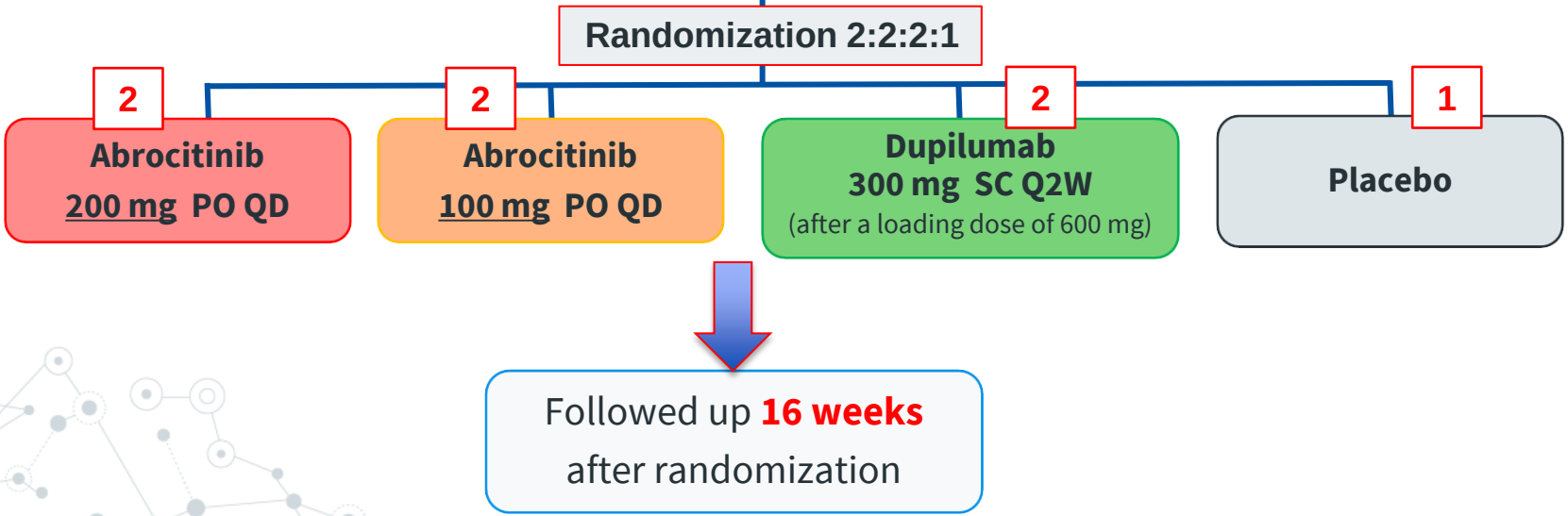
6) If receiving concomitant medications for any reason other than AD, must be on a stable regimen

Patients – Exclusion criteria

1) **Previously used systemic JAK inhibitors or dupilumab**
2) A medical history of conditions associated with **thrombocytopenia, coagulopathy, or platelet dysfunction**.
3) Receiving anti-coagulants or medications known to cause thrombocytopenia
4) Currently have **other inflammatory skin diseases or skin conditions**
5) Vaccinated or exposed to a live or attenuated vaccine within the 6 weeks
6) Participation in other studies involving investigational drug(s)
7) Known immunodeficiency disorder
8) History of lymphoma, leukemia or any lymphoproliferative disorder
9) Significant trauma or major surgery within 1 month

Study Procedures

- In a 28-day screening period, **systemic and topical medications for AD were discontinued**.
- **Emollients were used BID**, starting at least 7 days before randomization and **continued throughout the trial**.
- **Low- or medium-potency topical therapies were allowed during the trial**.
  - → topical glucocorticoids, topical calcineurin inhibitors, topical PDE4 inhibitors
- Patients were allowed to use more than one topical agent.



Outcomes Assessment

Primary End Points

- ✓ **IGA response at week 12**
  (a score of 0 or 1, with an improvement of ≥ 2 points from baseline)
- ✓ **EASI-75 response at week 12**
  (≥ 75% improvement from baseline)

Key Secondary End Points

- ✓ **Itch response at week 2**
  (≥ 4-point improvement from baseline in the score on the **PP-NRS**)
- ✓ **IGA responses at week 16**
- ✓ **EASI-75 responses at week 16**

Outcomes Assessment

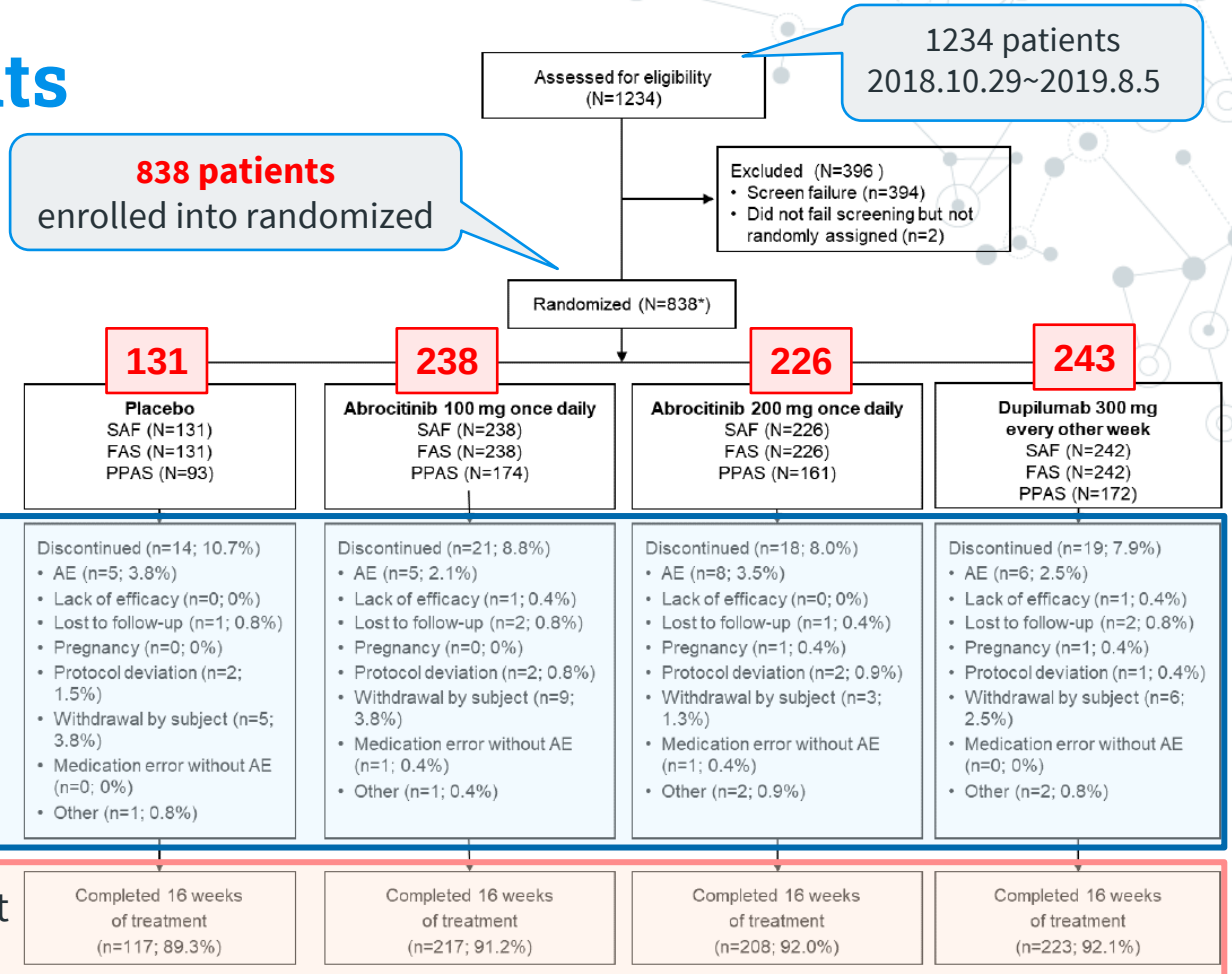
- Additional Secondary End Points
  - ✓ Improvements of at least 50%, at least 90%, and 100% in the score on the EASI
  - ✓ Time to itch response
  - ✓ Changes in percentage of BSA involvement
  - ✓ POEM (Patient-Oriented Eczema Measure)
  - ✓ PSAAD (Pruritus and Symptoms Assessment for Atopic Dermatitis)
  - ✓ DLQI (Dermatology Life Quality Index)
  - ✓ Hospital Anxiety and Depression Scale
  - ✓ SCORAD (Scoring of Atopic Dermatitis), improvements of at least 50% and 75%
  - ✓ Change in SCORAD subjective assessments of itch and sleep loss

Statistical Analysis

- A sample size of **700 patients**
  - ✓ Provide at least **96% power** to detect **20 %** or more difference between the abrocitinib dose groups and the placebo group with respect to **an IGA response at week 12.**
  - ✓ Provide at least **99% power** to detect **30 %** or more between-group difference with respect to **an EASI-75 response at week 12.**
- A sequential, **Bonferroni- based procedure** to control the family-wise type I error rate at 5%
  - ✓ **The two primary end points** were tested first for the higher dose of abrocitinib and then for the lower dose at a **significance level of 5%**
  - ✓ In the **key secondary end points**, the significance level was evenly split （**2.5% each**）
- **Modified intention-to-treat analysis**

Results – Patients

◎One patient randomly assigned to the dupilumab arm was not treated and was not included in the analysis sets.



Results – Patients

Table 1. Demographic and Disease Characteristics of the Patients at Baseline.*

Characteristic	Total (N=837)	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)	Placebo (N=131)
Age — yr	37.7±14.7	38.8±14.5	37.3±14.8	37.1±14.6	37.4±15.2
Female sex — no. (%)	428 (51.1)	122 (54.0)	118 (49.6)	134 (55.4)	54 (41.2)
Race — no. (%)†					
White	606 (72.4)	161 (71.2)	182 (76.5)	176 (72.7)	87 (66.4)
Black	35 (4.2)	9 (4.0)	6 (2.5)	14 (5.8)	6 (4.6)
Asian	178 (21.3)	53 (23.5)	48 (20.2)	46 (19.0)	31 (23.7)
Other	18 (2.2)	3 (1.3)	2 (0.8)	6 (2.5)	7 (5.3)
Duration of atopic dermatitis — yr	22.7±15.4	23.4±15.6	22.7±16.3	22.8±14.8	21.4±14.4
IGA score — no. (%)					
0, clear	0	0	0	0	0
1, almost clear	0	0	0	0	0
2, mild	0	0	0	0	0
V 3, moderate	541 (64.6)	138 (61.1)	153 (64.3)	162 (66.9)	88 (67.2)
V 4, severe	296 (35.4)	88 (38.9)	85 (35.7)	80 (33.1)	43 (32.8)
EASI score‡	30.9±12.8	32.1±13.1	30.3±13.5	30.4±12.0	31.0±12.6
Body-surface-area involvement — %	48.5±23.1	50.8±23.0	48.1±23.1	46.5±22.1	48.9±24.9
PP-NRS score§	7.3±1.7	7.6±1.5	7.1±1.7	7.3±1.7	7.1±1.8
SCORAD score¶	67.9±12.6	69.3±12.7	66.8±13.8	67.9±11.4	67.9±12.0
POEM score‖	21.1±5.5	21.5±5.3	20.9±5.5	21.2±5.5	20.4±6.1
DLQI score**	15.7±6.6	16.3±6.6	15.5±6.4	15.6±6.7	15.2±6.9
Coexisting medical conditions — no. (%)					
Asthma	284 (33.9)	82 (36.3)	79 (33.2)	75 (31.0)	48 (36.6)
Allergic conjunctivitis	79 (9.4)	18 (8.0)	21 (8.8)	26 (10.7)	14 (10.7)
Food allergy	125 (14.9)	39 (17.3)	36 (15.1)	36 (14.9)	14 (10.7)

The baseline characteristics of the patients were similar across groups.

Results – Primary end points

Table 2. Summary of Efficacy End Points.*

End Point	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)†	Placebo (N=131)
Primary end points				
IGA response at week 12 — no./total no. (%)‡	106/219 (48.4)	86/235 (36.6)	88/241 (36.5)	18/129 (14.0)
Difference from placebo (95% CI) — percentage points	34.8 (26.1 to 43.5)	23.1 (14.7 to 31.4)	22.5 (14.2 to 30.9)	NA
P value	<0.001	<0.001		
EASI-75 response at week 12 — no./total no. (%)§	154/219 (70.3)	138/235 (58.7)	140/241 (58.1)	35/129 (27.1)
Difference from placebo (95% CI) — percentage points	43.2 (33.7 to 52.7)	31.9 (22.2 to 41.6)	30.9 (21.2 to 40.6)	NA
P value	<0.001	<0.001		

Both 200 mg or 100 mg dose of Abrocitinib had **significant difference from placebo**

Results – Key Secondary end points

End Point Key secondary end points	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)†	Placebo (N=131)
Itch response at week 2 — no./total no. (%)¶	111/226 (49.1)	75/236 (31.8)	63/239 (26.4)	18/130 (13.8)
Difference from placebo (95% CI) — percentage points	34.9 (26.0 to 43.7)	17.9 (9.5 to 26.3)	12.5 (4.4 to 20.7)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI) — percentage points	22.1 (13.5 to 30.7)	5.2 (–2.9 to 13.4)	NA	NA
P value	<0.001	0.20‖		
IGA response at week 16 — no./total no. (%)	105/221 (47.5)	80/230 (34.8)	90/232 (38.8)	16/124 (12.9)
Difference from placebo (95% CI) — percentage points	35.0 (26.3 to 43.7)	22.1 (13.7 to 30.5)	25.6 (17.1 to 34.1)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI) — percentage points	9.4 (0.4 to 18.5)	–3.5 (–12.2 to 5.2)	NA	NA
EASI-75 response at week 16 — no./total no. (%)	157/221 (71.0)	138/229 (60.3)	152/232 (65.5)	38/124 (30.6)
Difference from placebo (95% CI) — percentage points	40.4 (30.4 to 50.4)	29.7 (19.5 to 39.9)	34.7 (24.6 to 44.8)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI)	5.5 (–3.1 to 14.1)	–5.1 (–13.9 to 3.7)	NA	NA

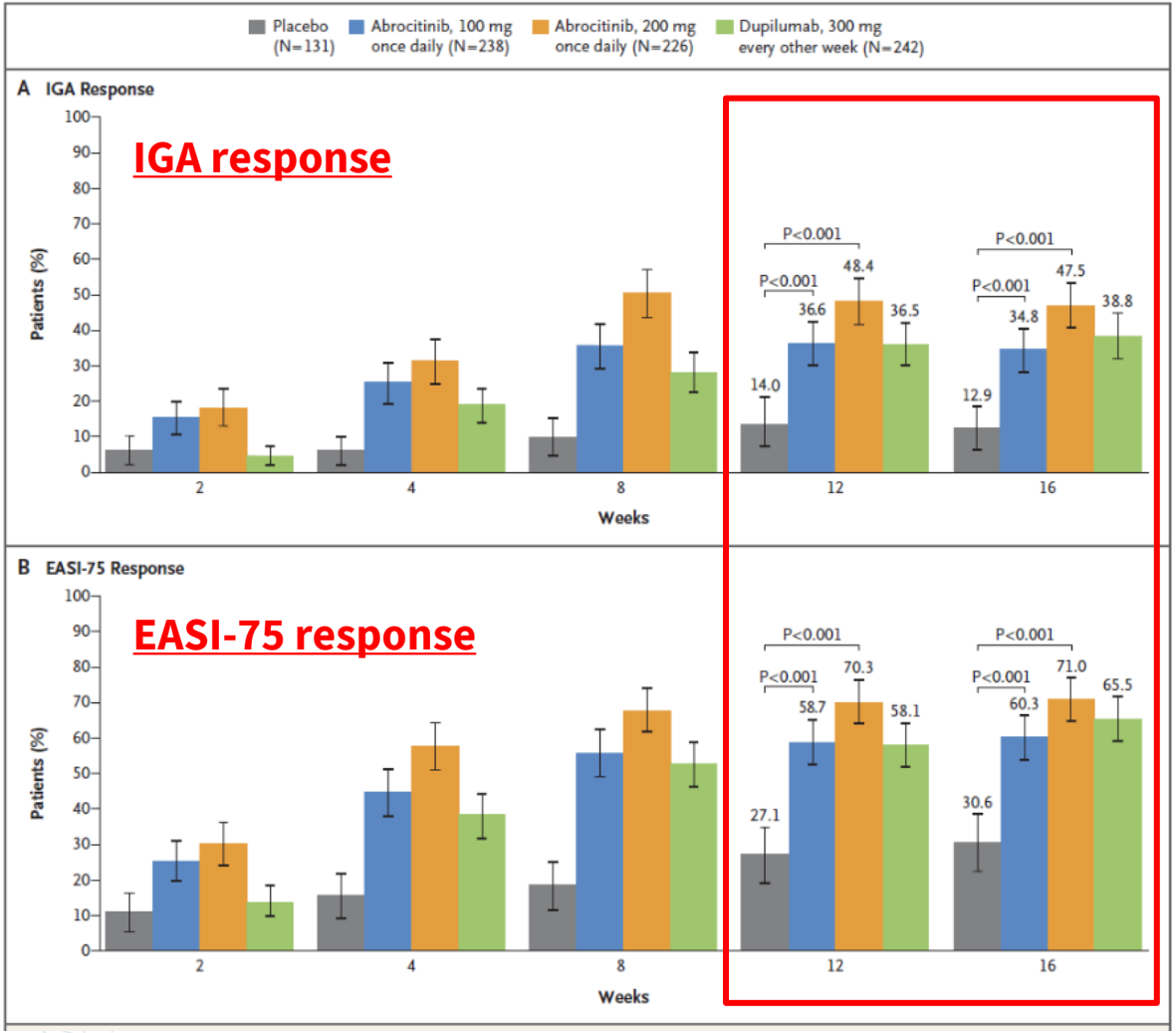
Both 200 mg or 100 mg dose of Abrocitinib had **significant difference from placebo**

Results – Key Secondary end points

End Point Key secondary end points	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)††	Placebo (N=131)
Itch response at week 2 — no./total no. (%)¶	111/226 (49.1)	75/236 (31.8)	63/239 (26.4)	18/130 (13.8)
Difference from placebo (95% CI) — percentage points	34.9 (26.0 to 43.7)	17.9 (9.5 to 26.3)	12.5 (4.4 to 20.7)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI) — percentage points	22.1 (13.5 to 30.7)	5.2 (–2.9 to 13.4)	NA	NA
P value	<0.001	0.20		
IGA response at week 16 — no./total no. (%)	105/221 (47.5)	80/230 (34.8)	90/232 (38.8)	
Difference from placebo (95% CI) — percentage points	35.0 (26.3 to 43.7)	22.1 (13.7 to 30.5)	25.6 (17.1 to 34.1)	
P value	<0.001	<0.001		
Difference from dupilumab (95% CI) — percentage points	9.4 (0.4 to 18.5)	–3.5 (–12.2 to 5.2)	NA	
EASI-75 response at week 16 — no./total no. (%)	157/221 (71.0)	138/229 (60.3)	152/232 (65.5)	38/124 (30.6)
Difference from placebo (95% CI) — percentage points	40.4 (30.4 to 50.4)	29.7 (19.5 to 39.9)	34.7 (24.6 to 44.8)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI)	5.5 (–3.1 to 14.1)	–5.1 (–13.9 to 3.7)	NA	NA

With respect to itch response at week 2, **only 200 mg** dose of Abrocitinib had **significant difference from dupilumab**

Results


Placebo (N=131)
Abrocitinib, 100 mg once daily (N=238)
Abrocitinib, 200 mg once daily (N=226)
Dupilumab, 300 mg every other week (N=242)
A IGA Response
IGA response
Patients (%)
Weeks
P<0.001
48.4
36.6
36.5
14.0
47.5
34.8
38.8
12.9
B EASI-75 Response
EASI-75 response
70.3
58.7
58.1
27.1
71.0
60.3
65.5
30.6

Results – Safety

✓ **No Deaths**

Table 3. Summary of Adverse Events.

Event	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)	Placebo (N=131)
	number of patients with event (percent)			
≥1 Adverse event	140 (61.9)	121 (50.8)	121 (50.0)	70 (53.4)
Serious adverse event*	2 (0.9)	6 (2.5)	2 (0.8)	5 (3.8)
Severe adverse event*	4 (1.8)	5 (2.1)	2 (0.8)	3 (2.3)
Adverse event leading to study discontinuation	10 (4.4)	6 (2.5)	8 (3.3)	5 (3.8)
Adverse event reported in ≥5% of patients in any group				
Nausea	25 (11.1)	10 (4.2)	7 (2.9)	2 (1.5)
Conjunctivitis	3 (1.3)	2 (0.8)	15 (6.2)	3 (2.3)
Nasopharyngitis 鼻咽炎	15 (6.6)	22 (9.2)	23 (9.5)	9 (6.9)
Upper respiratory tract infection	9 (4.0)	12 (5.0)	9 (3.7)	6 (4.6)
Headache	15 (6.6)	10 (4.2)	13 (5.4)	6 (4.6)
Acne	15 (6.6)	7 (2.9)	3 (1.2)	0
Herpes zoster†	4 (1.8)	2 (0.8)	0	0
Thrombocytopenia†	2 (0.9)	0	0	0

Results – Safety

Event	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)	Placebo (N=131)
	number of patients with event (percent)			
Adverse event reported in ≥5% of patients in any group				
Nausea	25 (11.1)	10 (4.2)	7 (2.9)	2 (1.5)
Conjunctivitis 結膜炎	3 (1.3)	2 (0.8)	15 (6.2)	3 (2.3)
Nasopharyngitis 鼻咽炎	15 (6.6)	22 (9.2)	23 (9.5)	9 (6.9)
Upper respiratory tract infection	9 (4.0)	12 (5.0)	9 (3.7)	6 (4.6)
Headache	15 (6.6)	10 (4.2)	13 (5.4)	6 (4.6)
Acne	15 (6.6)	7 (2.9)	3 (1.2)	0
Herpes zoster†	4 (1.8)	2 (0.8)	0	0
Thrombocytopenia†	2 (0.9)	0	0	0

Three serious infections were reported **2 patients (0.8%)** in the **100-mg abrocitinib.**

- ✓ **Pneumonia** and **herpes labialis** (withdrawn from the trial because of pneumonia)
- ✓ **Infectious diarrhea**

Discussion

Discussion

- In contrast to previous clinical trials that evaluated abrocitinib as monotherapy in patients with AD, in the current trial, we evaluated abrocitinib in patients with AD who were receiving **background therapy with topical medications**.

Efficacy

- **Compared to Placebo**

  Both 200 mg or 100 mg dose of abrocitinib resulted in significantly greater effect on the basis of IGA and EASI-75 responses at weeks 12 and 16 and itch response at week 2.

- **Compared to Dupilumab**

  → The **100 mg dose of abrocitinib had similar outcomes** with dupilumab.

  → The **200 mg dose of abrocitinib was superior to dupilumab only with respect to itch response at week 2.**

Discussion

Safety

1) **Adverse events** occurred in a **higher** **percentage of patients in the** **200 mg abrocitinib group** than in the placebo or the dupilumab group.
2) The percentages of patients who had adverse events in **the 100 mg abrocitinib group were similar to dupilumab group.**

3) The **main adverse events with abrocitinib** were **nausea, acne, nasopharyngitis, and headache.**
4) **Conjunctivitis** **occurred more frequently with** **dupilumab** than with placebo, as has been reported in previous trials.
5) **Serious and opportunistic infections** are considered to be a risk with **JAK inhibitors**.

Herpes zoster was reported more frequently with abrocitinib than with placebo or dupilumab, and **serious infections** occurred in two patients receiving abrocitinib.

Limitations

1) **Short follow-up period**.
2) **Involved only adults.**
3) Not formally designed to evaluate the superiority over dupilumab.
4) Lack of a plan for adjustment of confidence intervals.
5) Patients who withdrew from the trial may have introduced bias.
6) **Sponsor (Pfizer) designed the trial, collected and analyzed the data.**

Appraisal

CASP RCT Checklist

Section A:
Is the basic study design valid for a randomised controlled trial?

1. Did the study address a clearly focused research question?

☑ Yes ☐ No ☐ Can't tell

P patient	Adults with moderate-to-severe atopic dermatitis who were receiving background topical therapy
I intervention	Abrocitinib 100mg or 200mg
C comparison	Dupilumab or Placebo
O outcome	efficacy and safety

2. Was the assignment of participants to interventions randomised?

☑ Yes ☐ No ☐ Can't tell

- Patients were randomly assigned in a 2:2:2:1 ratio to receive 200 mg or 100 mg of abrocitinib orally once daily, 300 mg of dupilumab subcutaneously every other week (after a loading dose of 600 mg), or placebo for 16 weeks.
- The patients, investigators, and representatives of the sponsor were unaware of the trial-group assignments.

Section A:
Is the basic study design valid for a randomised controlled trial?

3. Were all participants who entered the study accounted for at its conclusion?

☐ Yes ☑ No ☐ Can't tell

- The primary analysis of efficacy was performed in the modified intention-to treat-population, which included all the patients who had undergone randomization and received at least 1 dose of a trial drug or placebo.
- One patient randomly assigned to the dupilumab arm was not treated and was not included in the analysis sets.

Patients, no. (%)	Abrocitinib 200 mg once daily (N=226)	Abrocitinib 100 mg once daily (N=238)	Dupilumab 300 mg every other week (N=243)	Placebo (N=131)
Screened: 1234	—	—	—	—
Screen failure: 394	—	—	—	—
Not screen failure but not randomly assigned: 2	—	—	—	—
Randomly assigned	226 (100.0)	238 (100.0)	243 (100.0)	131 (100.0)
Treated	226 (100.0)	238 (100.0)	242 (99.6)	131 (100.0)
Not treated	0	0	1 (0.4)	0
Safety analysis set	226 (100.0)	238 (100.0)	242 (99.6)	131 (100.0)
Efficacy full analysis set (FAS)	226 (100.0)	238 (100.0)	242 (99.6)	131 (100.0)
Efficacy per protocol analysis set (PPAS)	161 (71.2)	174 (73.1)	172 (70.8)	93 (71.0)

Section A:
Is the basic study design valid for a randomised controlled trial?

3. Were all participants who entered the study accounted for at its conclusion?

☐ Yes ☑ No ☐ Can't tell

Denominators differ at each end point and at each visit because assessments for that end point were missing for the patients who either missed that visit or attended the visit outside the prespecified window.

Table 2. Summary of Efficacy End Points.*

End Point	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)†	Placebo (N=131)
Primary end points				
IGA response at week 12 — no./total no. (%)‡	106/219 (48.4)	86/235 (36.6)	88/241 (36.5)	18/129 (14.0)
Difference from placebo (95% CI) — percentage points	34.8 (26.1 to 43.5)	23.1 (14.7 to 31.4)	22.5 (14.2 to 30.9)	NA
P value	<0.001	<0.001		
EASI-75 response at week 12 — no./total no. (%)§	154/219 (70.3)	138/235 (58.7)	140/241 (58.1)	35/129 (27.1)
Difference from placebo (95% CI) — percentage points	43.2 (33.7 to 52.7)	31.9 (22.2 to 41.6)	30.9 (21.2 to 40.6)	NA
P value	<0.001	<0.001		
Key secondary end points				
Itch response at week 2 — no./total no. (%)¶	111/226 (49.1)	75/236 (31.8)	63/239 (26.4)	18/130 (13.8)
Difference from placebo (95% CI) — percentage points	34.9 (26.0 to 43.7)	17.9 (9.5 to 26.3)	12.5 (4.4 to 20.7)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI) — percentage points	22.1 (13.5 to 30.7)	5.2 (–2.9 to 13.4)	NA	NA
P value	<0.001	0.20		
IGA response at week 16 — no./total no. (%)	105/221 (47.5)	80/230 (34.8)	90/232 (38.8)	16/124 (12.9)
Difference from placebo (95% CI) — percentage points	35.0 (26.3 to 43.7)	22.1 (13.7 to 30.5)	25.6 (17.1 to 34.1)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI) — percentage points	9.4 (0.4 to 18.5)	–3.5 (–12.2 to 5.2)	NA	NA
EASI-75 response at week 16 — no./total no. (%)	157/221 (71.0)	138/229 (60.3)	152/232 (65.5)	38/124 (30.6)
Difference from placebo (95% CI) — percentage points	40.4 (30.4 to 50.4)	29.7 (19.5 to 39.9)	34.7 (24.6 to 44.8)	NA
P value	<0.001	<0.001		
Difference from dupilumab (95% CI)	5.5 (–3.1 to 14.1)	–5.1 (–13.9 to 3.7)	NA	NA

Section B:
Was the study methodologically sound?

4. Were the participants ‘blind’ to intervention they were given?

☑ Yes ☐ No ☐ Can’t tell

Were the investigators ‘blind’ to the intervention they were giving to participants?

☑ Yes ☐ No ☐ Can’t tell

Were the people assessing/analyzing outcome/s ‘blinded’?

☑ Yes ☐ No ☐ Can’t tell

- The patients, investigators, and representatives of the sponsor were unaware of the trial-group assignments.

Section B:
Was the study methodologically sound?

5. Were the study groups similar at the start of the randomised controlled trial?

☑ Yes ☐ No ☐ Can't tell

- The baseline characteristics of the patients, including previous medication use, were similar across groups.

Section B:
Was the study methodologically sound?

6. Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?

☑ Yes ☐ No ☐ Can't tell

- **Emollients were used twice daily**, starting at least 7 days before randomization and continued throughout the trial.
- **Low- or medium-potency topical therapies were allowed** during the trial.

Table S5. Summary of Medicated Background Topical Therapy Used Within Treatment Period

	Total (N=837)	Abrocitinib 200 mg once daily (N=226)	Abrocitinib 100 mg once daily (N=238)	Dupilumab 300 mg every other week (N=242)	Placebo (N=131)
Duration in days					
Mean (SD)	79.7 (42.2)	77.7 (42.0)	78.1 (43.4)	79.9 (42.7)	85.7 (39.4)
Median (Q1, Q3)	109.0 (35.0, 112.0)	107.5 (31.0, 112.0)	110.0 (30.0, 112.0)	109.0 (33.0, 112.0)	110.0 (57.0, 112.0)
Range	(0.0, 149.0)	(0.0, 149.0)	(0.0, 128.0)	(0.0, 128.0)	(0.0, 132.0)
Proportion of patients who used medicated topical therapy, %	787 (94.0)	216 (95.6)	223 (93.7)	226 (93.4)	122 (93.1)
Proportion who discontinued medicated topical therapy during study treatment, %	209 (26.6)	67 (31.0)	60 (26.9)	60 (26.5)	22 (18.0)
Proportion of patients who used medicated topical therapy on study day 1, %	691 (82.6)	186 (82.3)	193 (81.1)	206 (85.1)	106 (80.9)
Proportion who discontinued for at least 1 week, %	199 (25.3)	67 (31.0)	56 (25.1)	56 (24.8)	20 (16.4)

Section C:
What are the results?

7. Were the effects of intervention reported comprehensively?

☐ Yes ☑ No ☐ Can't tell

- The trial was not formally designed to evaluate the superiority of abrocitinib over dupilumab with respect to the two primary end points.

- "We determined that a sample size of 700 patients would provide the trial with at least 96% power to detect a difference of 20 or more percentage points between the abrocitinib dose groups and the placebo group ....."

Efficacy full analysis (N=837)
Abrocitinib 200 mg (N=226)
Abrocitinib 100 mg (N=238)
Dupilumab 300 mg (N=242)
Placebo (N=131)

Section C:
What are the results?

8. Was the precision of the estimate of the intervention or treatment effect reported?

☑ Yes ☐ No ☐ Can't tell

9. Do the benefits of the experimental intervention outweigh the harms and costs?

☐ Yes ☐ No ☑ Can't tell

Benefits	Greater efficacy (200 mg) Oral formulation
Harms	Adverse events Daily used

Section D:
Will the results help locally?

10. Can the results be applied to your local population/in your context?

☑ Yes ☐ No ☐ Can't tell

Table 1. Demographic and Disease Characteristics of the Patients at Baseline.*

Characteristic	Total (N=837)	Abrocitinib, 200 mg Once Daily (N=226)	Abrocitinib, 100 mg Once Daily (N=238)	Dupilumab, 300 mg Every Other Week (N=242)	Placebo (N=131)
Age — yr	37.7±14.7	38.8±14.5	37.3±14.8	37.1±14.6	37.4±15.2
Female sex — no. (%)	428 (51.1)	122 (54.0)	118 (49.6)	134 (55.4)	54 (41.2)
Race — no. (%)†					
White	606 (72.4)	161 (71.2)	182 (76.5)	176 (72.7)	87 (66.4)
Black	35 (4.2)	9 (4.0)	6 (2.5)	14 (5.8)	6 (4.6)
Asian	178 (21.3)	53 (23.5)	48 (20.2)	46 (19.0)	31 (23.7)
Other	18 (2.2)	3 (1.3)	2 (0.8)	6 (2.5)	7 (5.3)
Duration of atopic dermatitis — yr	22.7±15.4	23.4±15.6	22.7±16.3	22.8±14.8	21.4±14.4

	Abrocitinib 200 mg once daily (N=226)	Abrocitinib 100 mg once daily (N=238)	Dupilumab 300 mg every other week (N=243)	Placebo (N=131)
US/Canada/Australia, n (%)				
Australia	9 (4.0)	9 (3.8)	11 (4.5)	9 (6.9)
Canada	9 (4.0)	9 (3.8)	10 (4.1)	8 (6.1)
United States	47 (20.8)	47 (19.7)	53 (21.8)	26 (19.8)
Europe, n (%)				
Germany	13 (5.8)	17 (7.1)	15 (6.2)	10 (7.6)
Italy	2 (0.9)	1 (0.4)	0	0
Spain	1 (0.4)	2 (0.8)	3 (1.2)	0
UK	18 (8.0)	20 (8.4)	20 (8.2)	9 (6.9)
Bulgaria	5 (2.2)	5 (2.1)	4 (1.6)	2 (1.5)
Czech Republic	15 (6.6)	14 (5.9)	16 (6.6)	10 (7.6)
Hungary	2 (0.9)	3 (1.3)	7 (2.9)	3 (2.3)
Latvia	2 (0.9)	4 (1.7)	3 (1.2)	0
Poland	47 (20.8)	57 (23.9)	50 (20.6)	28 (21.4)
Slovakia	4 (1.8)	2 (0.8)	7 (2.9)	2 (1.5)
Asia, n (%)				
Japan	25 (11.1)	19 (8.0)	21 (8.6)	11 (8.4)
Korea	11 (4.9)	9 (3.8)	8 (3.3)	5 (3.8)
Taiwan	5 (2.2)	6 (2.5)	4 (1.6)	1 (0.8)
Latin America, n (%)				
Chile	8 (3.5)	9 (3.8)	8 (3.3)	5 (3.8)
Mexico	3 (1.3)	5 (2.1)	3 (1.2)	2 (1.5)

Section D:
Will the results help locally?

11. Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?

☐ Yes ☐ No ☑ Can't tell

- In terms of atopic dermatitis as a lifelong disease, this 16-week trial did not establish the **long-term efficacy and safety** of abrocitinib.
- The trial was not formally designed to **evaluate the superiority of abrocitinib over dupilumab** with respect to the two primary end points.
- Data from **head-to-head trials with other JAK inhibitors** are lacking.

Question

是否同意Abrocitinib長期使用在
中度至重度的異位性皮膚炎患者？

同意

需要更多
文獻支持

不同意

Q & A

Thank You