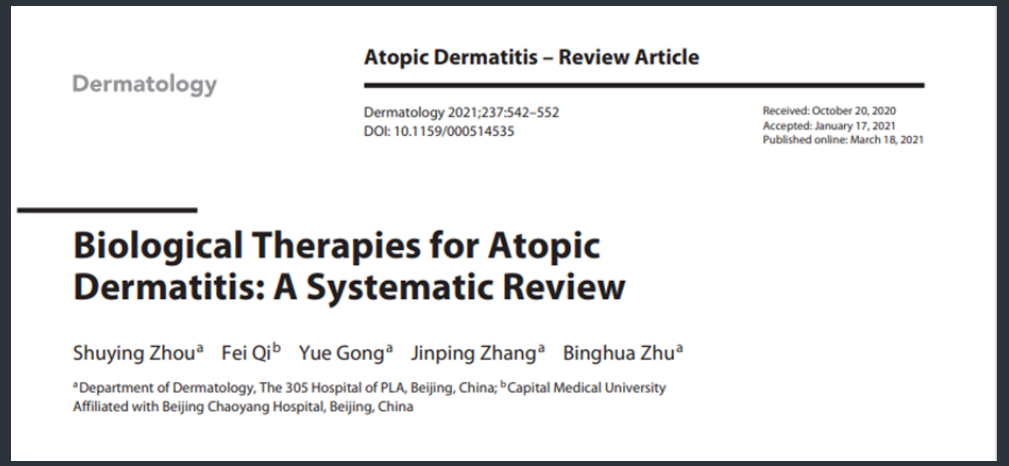
Atopik Dermatit Tedavisinde JAK İnhibitörleri

Doç. Dr. Özge Aşkın
İÜC-Cerrahpaşa Tıp Fakültesi

Atopik Dermatit Tedavisi

Biyolojikler	Jak İnh
• Dupilumab • Lebrikizumab • Tralokinumab • Nemolizumab	• Barisitinib • Upadasitinib • Abrositinib • Delgositinib • Ruksolitinib



Dermatology

Atopic Dermatitis – Review Article

Dermatology 2021;237:542–552
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Biological Therapies for Atopic Dermatitis: A Systematic Review

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THE JOURNAL OF DERMATOLOGY

doi: 10.1111/1346-8138.15504

Journal of Dermatology 2021; **48**: 152–157

REVIEW ARTICLE

Emerging treatments for atopic dermatitis

Norito KATOH

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JAK inhibitörleri

JAK–STAT yolağının inhibisyonu, bir çok sitokinin sinyal aktivasyonunun **kısmi ve geri döndürülebilir modülasyonuna** izin vermektedir.[1,2]

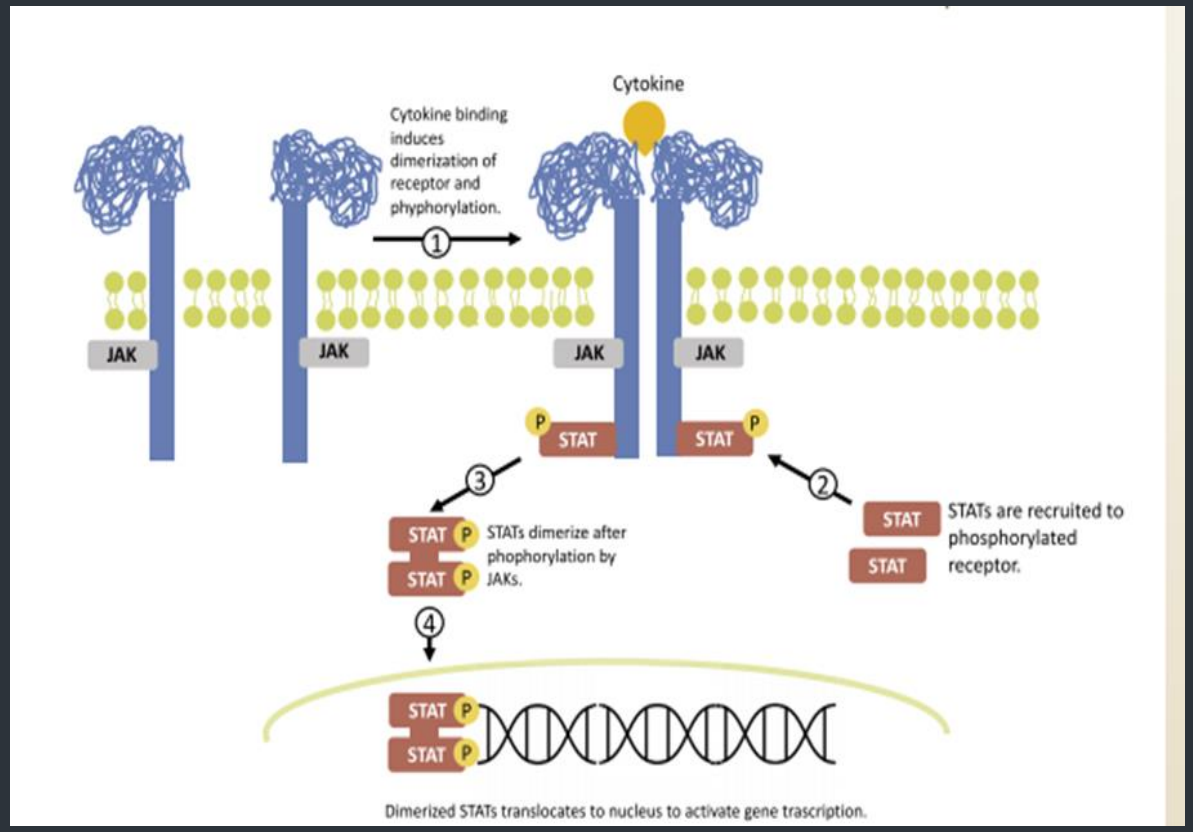
Hedefe yönelik sistemik tedavilerdeki bu farklı yaklaşımlar, inflamasyon döngüsünü bozmaktadır.

Biyolojikler

Genel olarak biyolojikler, **tek bir sitokine** veya reseptöre bağlanarak onların uzun dönem **inhibe edilmesini** sağlar.[1,2]

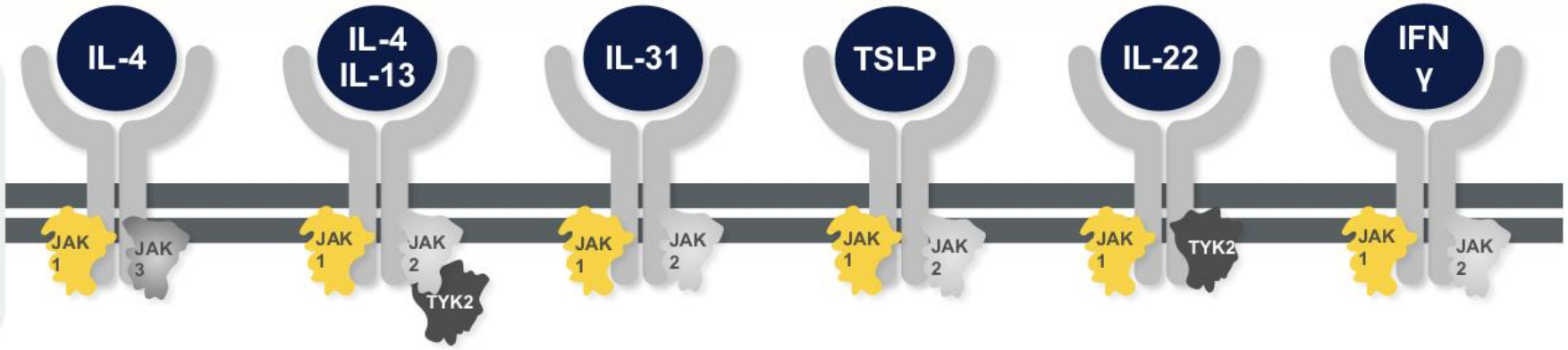
JAK-STAT YOLAĞI

- Sitokin ⟷ Hücre zarı üzerindeki reseptöre bağlandığında
- Hücre içi JAK proteinleri aktive olur.
- STAT proteinleri JAK tarafından fosfat bağlanarak aktifleştirilir
- Aktifleşen STAT proteinleri hücre çekirdeğine gelirler
- JAK sinyali, hücresel yanıt ve fonksiyonlar ile sonuçlanır:
  - Proliferasyon
  - Diferansiyasyon
  - Migrasyon
  - Apoptoz
  - Hücre sağkalımı



JAK-STAT yolağı üzerinden birçok sitokin AD patogenezini tetikler

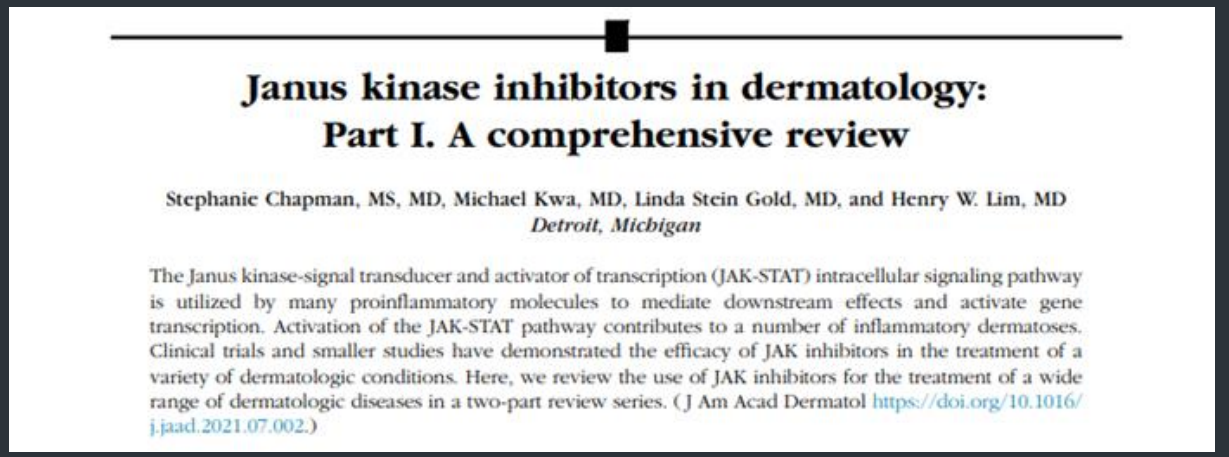
Farklı sitokin reseptör aileleri, sinyal transdüksiyonu için JAK izoform çiftlerini kullanmaktadır.[1,2]



	IL-4	IL-4 IL-13	IL-31	TSLP	IL-22	IFN γ
İnflamasyonun artması[2,3]	✓	✓	✓	✓		✓
Kaşıntının ve altta yatan kaşınmanın artması[2]	✓	✓	✓	✓	✓	
Cilt bariyerinin bozulması[2]	✓	✓			✓	
Cilt mikrobiyomu Disbiosis[2]	✓	✓				
Epidermal kalınlaşma[2,4]	✓				✓	

Atopik Dermatitte JAK İnhibitörleri

- Barisitinib… JAK 1ve 2 inh- oral
- Abrositinib… selektif JAK 1 inh- oral
- Upadasitinib… selektif JAK 1 inh- oral

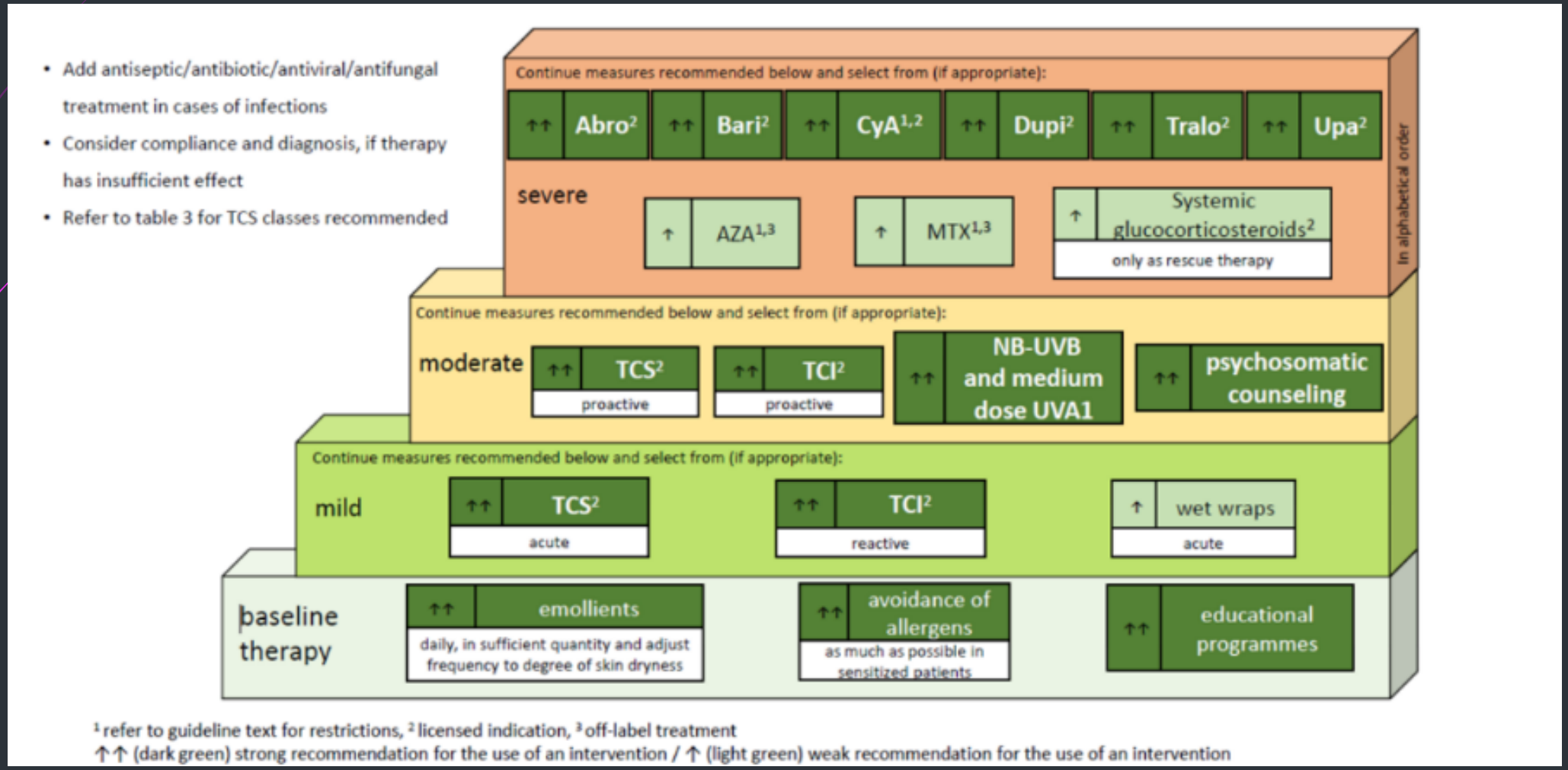


Janus kinase inhibitors in dermatology: Part I. A comprehensive review

Stephanie Chapman, MS, MD, Michael Kwa, MD, Linda Stein Gold, MD, and Henry W. Lim, MD
Detroit, Michigan

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) intracellular signaling pathway is utilized by many proinflammatory molecules to mediate downstream effects and activate gene transcription. Activation of the JAK-STAT pathway contributes to a number of inflammatory dermatoses. Clinical trials and smaller studies have demonstrated the efficacy of JAK inhibitors in the treatment of a variety of dermatologic conditions. Here, we review the use of JAK inhibitors for the treatment of a wide range of dermatologic diseases in a two-part review series. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2021.07.002.)

EuroGuiDerm Güncel AD Tedavi Kılavuzu 2022



[1] refer to guideline text for restrictions, [2] licensed indication, [3] off-label treatment
↑↑ (dark green) strong recommendation for the use of an intervention / ↑ (light green) weak recommendation for the use of an intervention

	Dupilumab	Barisitinib	Abrositinib	Upadasitinib
FDA Endikasyon	6<yaş, M2S AD	Endikasyonu onaylanmadı.	12<yaş M2S AD	12<yaş M2S AD
EMA Endikasyon	12<yaş, M2S AD	18<yaş M2S AD	18<yaş M2S AD	12<yaş M2S AD
MoA	Anti-IL-4/IL-13	JAK1/2 inhibitörü	Selektif JAK1 inhibitörü	Selektif JAK1 inhibitörü
Form	Subkutan enjeksiyon	Oral	Oral	Oral
Doz	300mg Q2W	2 mg ve 4 mg QD	100 mg ve 200 mg QD	15 mg ve 30 mg QD
Cevap zamanı	4-6 hafta	1-2 hafta	1-2 hafta	1-2 hafta
İzlem	Gerekmez	Tam kan sayımı, lipidler, KC	Tam kan sayımı, lipidler, KC	Tam kan sayımı, lipidler, KC
Sık görülen tedavi ilişkili advers etkiler	Konjuktivit, USYE, Artralji	USYE, LDL'de artış, trombositoz, bulantı, abdominal ağrı, herpes virus enfeksiyonları, akne	USYE, LDL'de artış, trombositopeni, kreatin fosfokinaz artışı, bulantı, abdominal ağrı, herpes virus enfeksiyonları, akne	USYE, baş ağrısı, LDL'de artış, anemi, nötropeni, kreatin kinaz artışı, bulantı, abdominal ağrı, herpes virus enfeksiyonları, akne
Faz-III Klinik Çalışmalar	5	8	8 (1- Dupilumab ile kafa-kafaya karşılaştırmalı)	6 (1- Dupilumab ile kafa-kafaya karşılaştırmalı)

GUIDELINE

European guideline (EuroGuiDerm) on atopic eczema: part I – systemic therapy

A. Wollenberg,[1,2,*] M. Kinberger,[3] B. Arents,[4] N. Aszodi,[1] G. Avila Valle,[3] S. Barbarot,[5] T. Bieber,[6] H.A. Brough,[7,8] P. Calzavara Pinton,[9] S. Christen-Zäch,[10] M. Deleuran,[11] M. Dittmann,[3] C. Dressler,[3] A.H. Fink-Wagner,[12] N. Fosse,[13] K. Gáspár,[14] L. Gerbens,[15] U. Gieler,[16] G. Girolomoni,[17] S. Gregoriou,[18] C.G. Mortz,[19] A. Nast,[3] U. Nygaard,[20] M. Redding,[21] E.M. Rehbinder,[22] J. Ring,[23] M. Rossi,[24] E. Serra-Baldrich,[25] D. Simon,[26] Z.Z. Szalai,[27] J.C. Szepietowski,[28] A. Torrelo,[29] T. Werfel,[30] C. Flohr[31,32,*]

Tedaviye başlamadan önce

- Tam kan sayımı
- Karaciğer fonksiyon testi
- Böbrek fonksiyon testi
- Lipid profili
- Kreatin fosfokinaz seviyesi
- AC grafisi
- Hepatit, HIV serolojisi
- Tüberküloz taraması

Takiplerinde

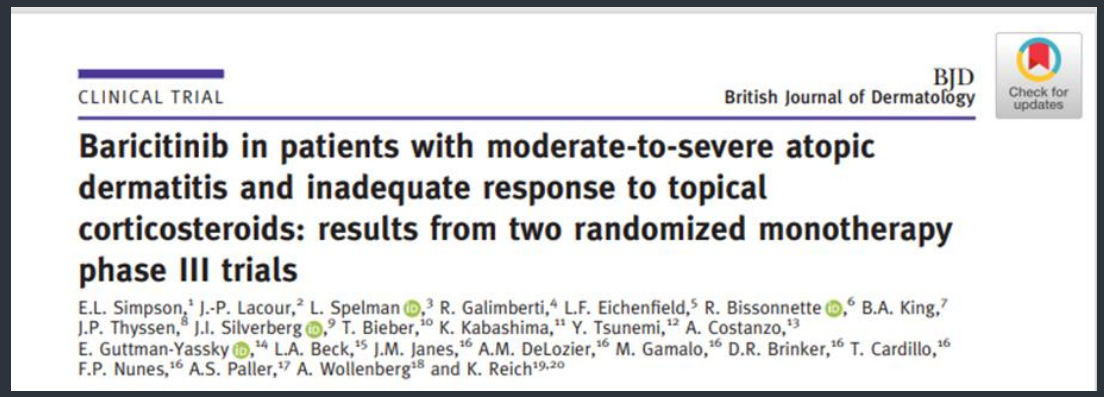
Tedavinin 4. haftası

- Tam kan sayımı
- Karaciğer fonksiyon testi
- Böbrek fonksiyon testi
- Lipid profili
- Kreatin fosfokinaz seviyesi

Her üç ayda bir yukarıdaki tetkikler tekrar edilmeli

Barisitinib

- Oral, küçük moleküllü, seçici JAK1 ve JAK2 inhibitörü
- Faz III çalışmaları
  - BREEZE-AD1 ve BREEZE-AD2



CLINICAL TRIAL

BJD
British Journal of Dermatology

Check for updates

Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: results from two randomized monotherapy phase III trials

E.L. Simpson,[1] J.-P. Lacour,[2] L. Spelman,[3] R. Galimberti,[4] L.F. Eichenfield,[5] R. Bissonnette,[6] B.A. King,[7] J.P. Thyssen,[8] J.I. Silverberg,[9] T. Bieber,[10] K. Kabashima,[11] Y. Tsunemi,[12] A. Costanzo,[13] E. Guttman-Yassky,[14] L.A. Beck,[15] J.M. Janes,[16] A.M. DeLozier,[16] M. Gamalo,[16] D.R. Brinker,[16] T. Cardillo,[16] F.P. Nunes,[16] A.S. Paller,[17] A. Wollenberg[18] and K. Reich[19,20]

- BREEZE AD-1 (624 hasta) ve AD-2 (615) iki farklı faz III çalışması
- Plasebo/1 gr/2 gr/4 gr barisitinib 16 hafta
- EASI75 cevabında ve AD uyku ölçeğinde anlamlı fark plaseboya göre
- Kaşıntıda 4 mg'da 1 haftada, 2mg'da 2 haftada belirgin azalma

Clinical Trial > JAMA Dermatol. 2020 Dec 1;156(12):1333-1343.
doi: 10.1001/jamadermatol.2020.3260.

Efficacy and Safety of Baricitinib Combined With Topical Corticosteroids for Treatment of Moderate to Severe Atopic Dermatitis: A Randomized Clinical Trial

Kristian Reich [1 2], Kenji Kabashima [3 4], Ketty Peris [5], Jonathan I Silverberg [6], Lawrence F Eichenfield [7 8], Thomas Bieber [9], Aleksandra Kaszuba [10], Jill Kolodsick [11], Fan E Yang [11], Margaret Gamalo [11], Dennis R Brinker [11], Amy M DeLozier [11], Jonathan M Janes [11], Fabio P Nunes [11], Jacob P Thyssen [12], Eric L Simpson [13]

- 329 orta şiddetli AD hastası
- 2 mg/ 4 mg barisitinib + topikal KS
- 16 hafta
- EASI90 cevabı plasebo için 14%, barisitinib 2 mg için 17%, barisitinib 4 mg için 24%

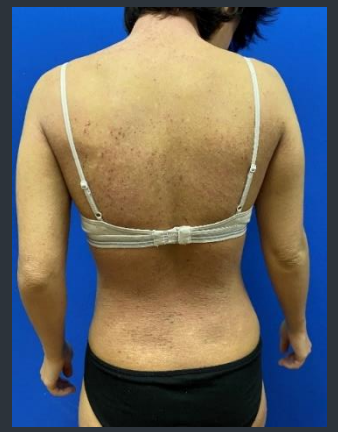
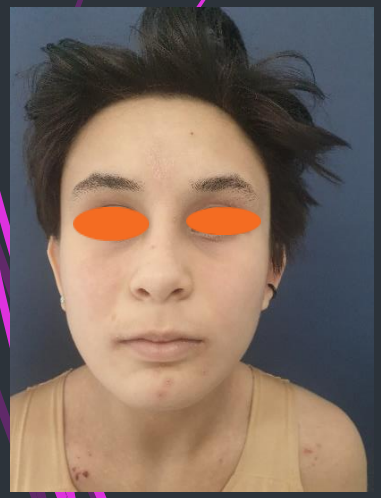
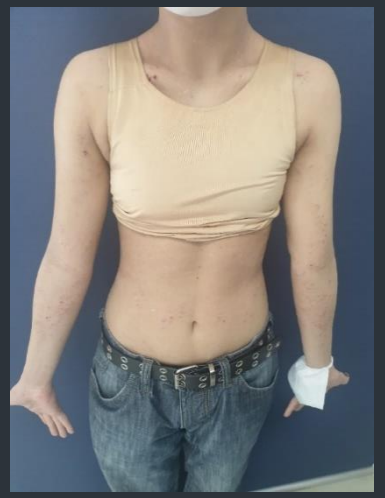
> JAMA Dermatol. 2021 Jun 1;157(6):691-699. doi: 10.1001/jamadermatol.2021.1273.

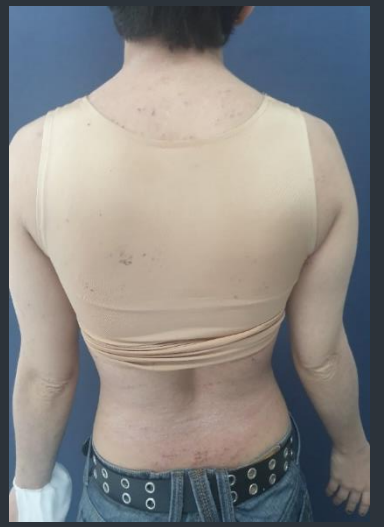
Long-term Efficacy of Baricitinib in Adults With Moderate to Severe Atopic Dermatitis Who Were Treatment Responders or Partial Responders: An Extension Study of 2 Randomized Clinical Trials

Jonathan I Silverberg [1], Eric L Simpson [2], Andreas Wollenberg [3], Robert Bissonnette [4], Kenji Kabashima [5 6], Amy M DeLozier [7], Luna Sun [7], Tracy Cardillo [7], Fabio P Nunes [8 9], Kristian Reich [10]

- BREEZE-AD3 uzun dönem etkililik çalışması
- 1081 hasta (plasebo-2 mg-4 mg barisitinib)
- EASI75 **16. haftada** %70, **68. haftada %55.7**
- Barisitinib uzun dönemde de orta-şiddetli AD'de etkililiğini koruyor



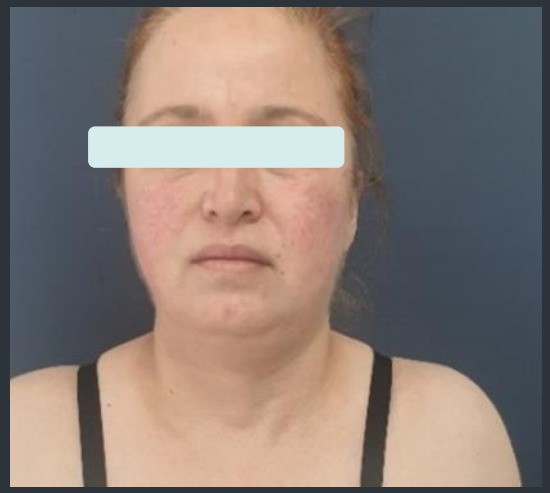





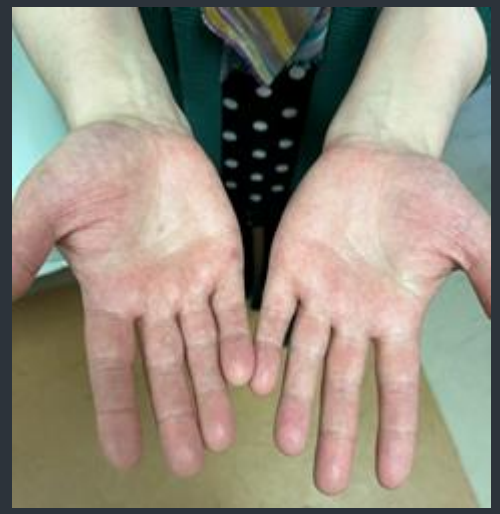


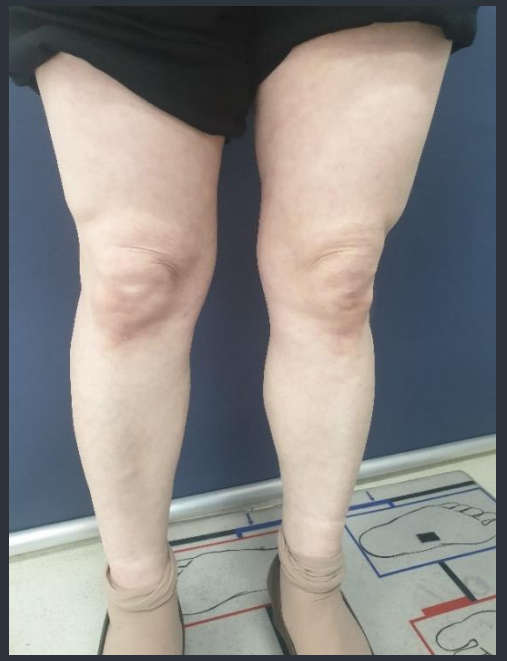
Başlangıç

3 ay

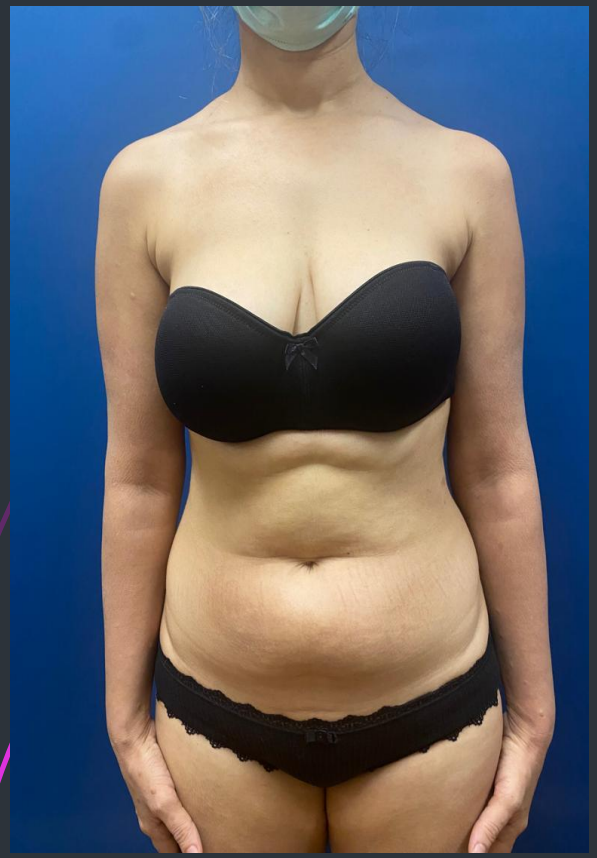
BAŞLANGIÇ





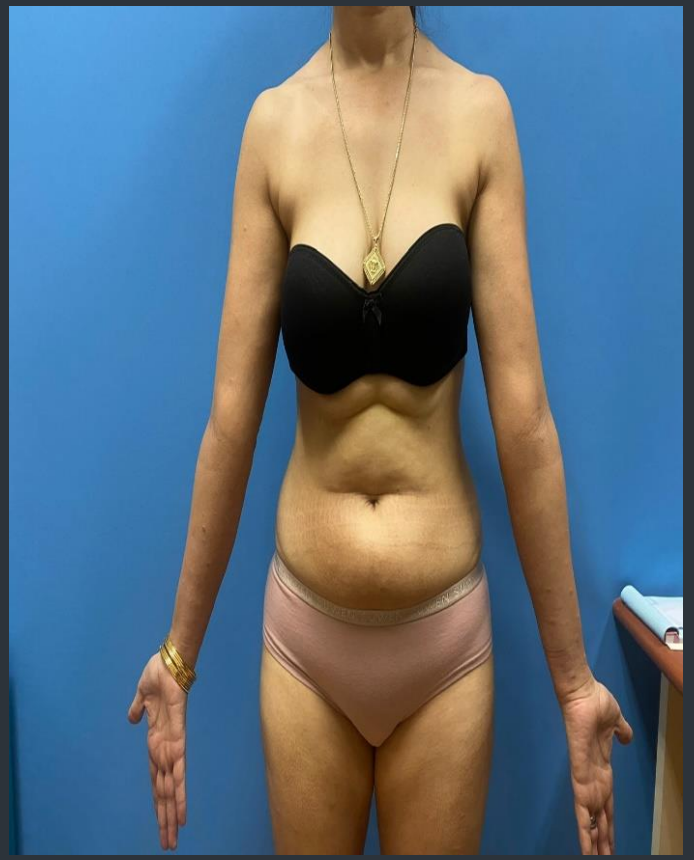


5. AY

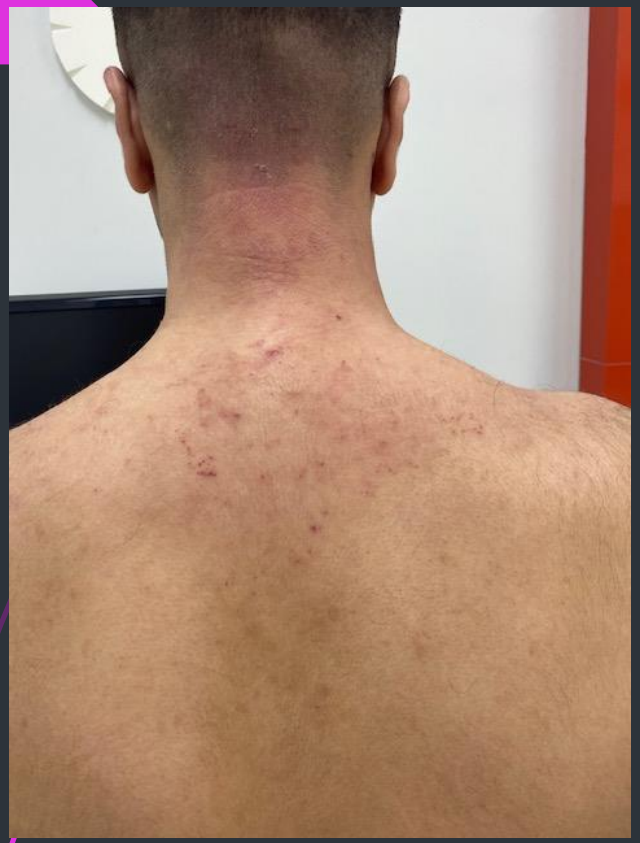


Başlangıç
SCORAD:40

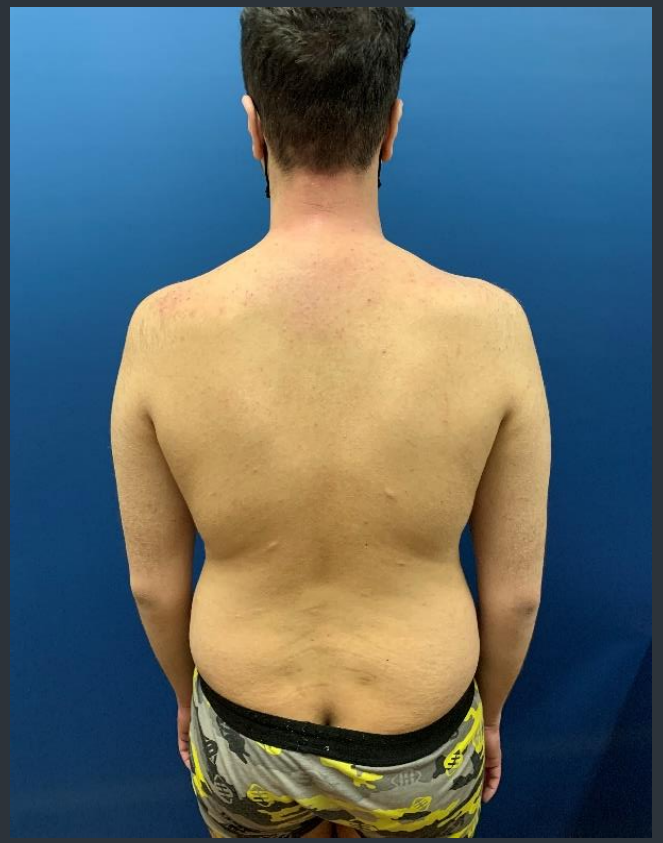
3.Ay
SCORAD:20,3



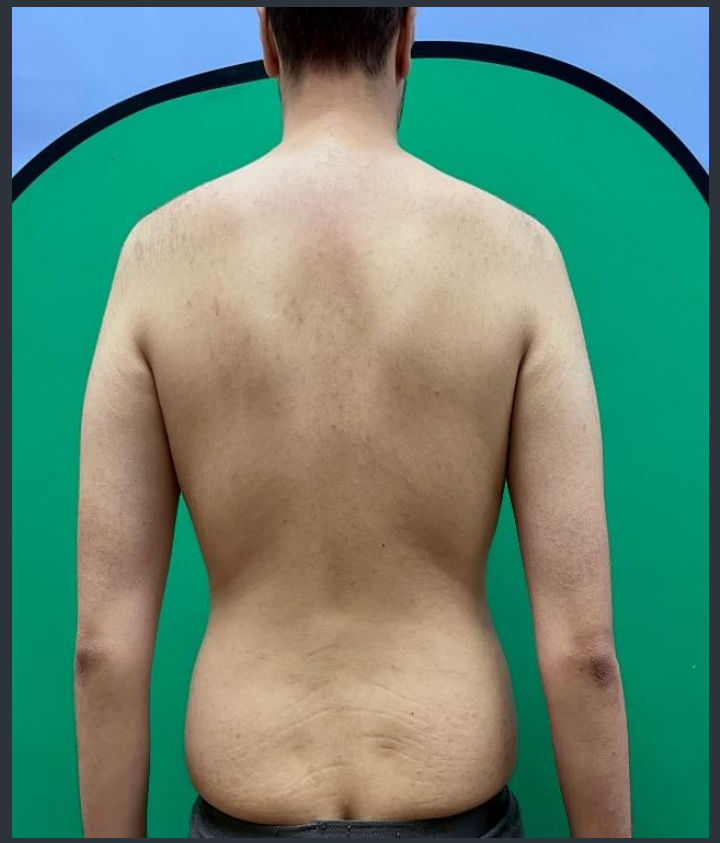
10. Ay
SCORAD:7,2



Başlangıç
SCORAD: 48,2



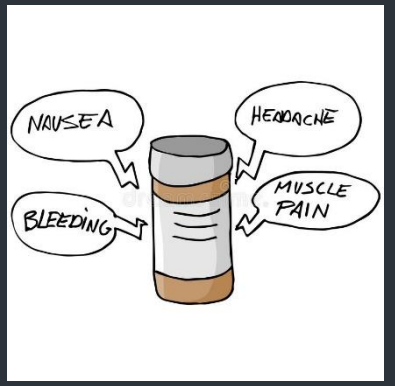
3. Ay
SCORAD: 25,6



10. Ay
SCORAD: 8

Barisitinib

- En sık görülen yan etkiler: ***Baş ağrısı, nazofarenjit***
  - Nötrofil düzeylerinde azalma, CK düzeylerinde yükselme, akne
- Venöz tromboembolizm, kardiovasküler yan etkiler, gastrointestinal perforasyon ve ciddi hematolojik değişiklikler bildirilmemiş



Upadasitinib

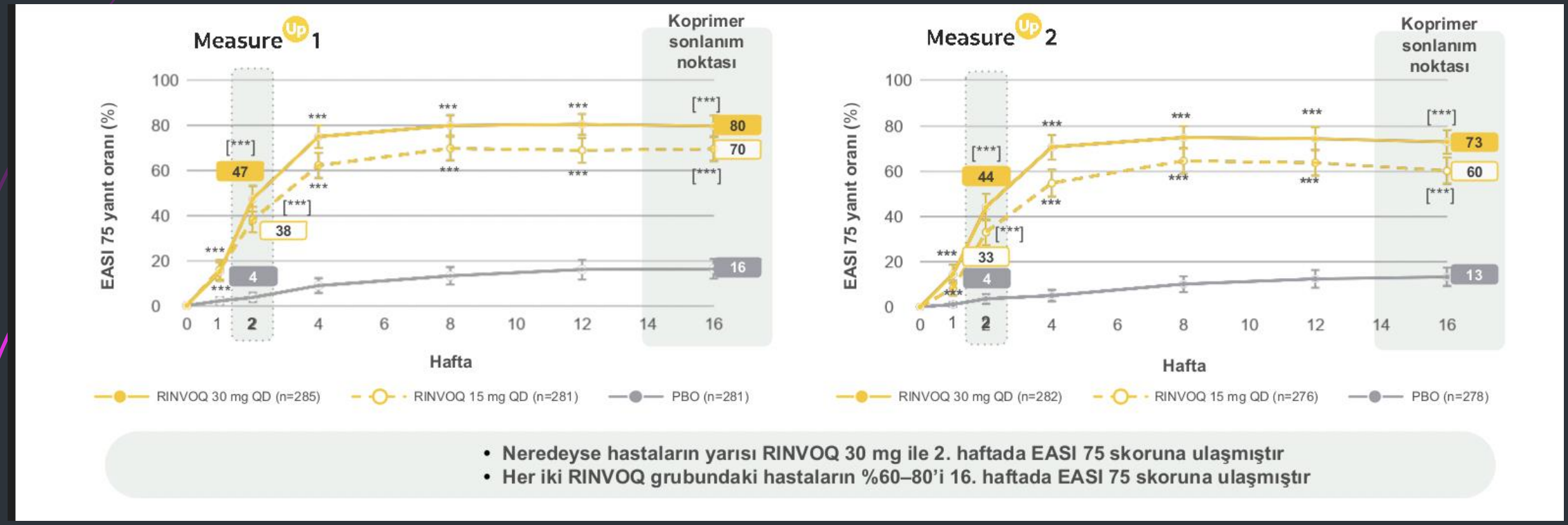
Efficacy and Safety of Upadacitinib in Patients With Moderate to Severe Atopic Dermatitis: Analysis of Follow-up Data From the Measure Up 1 and Measure Up 2 Randomized Clinical Trials

Eric L Simpson [1], Kim A Papp [2], Andrew Blauvelt [3], Chia-Yu Chu [4], H Chih-Ho Hong [5 6 7], Norito Katoh [8], Brian M Calimlim [9], Jacob P Thyssen [10], Albert S Chiou [11], Robert Bissonnette [12], Linda F Stein Gold [13], Colleen Wegzyn [9], Xiaofei Hu [9], Meng Liu [9], John Liu [9], Allan R Tenorio [9], Alvina D Chu [9], Emma Guttman-Yassky [14]

- Seçici JAK1 inhibitörü olan küçük molekül
- Faz 3 çalışması (MEASURE UP1 ve 2):
- 12 yaş ve üstü AD'li hastalarda
- Upadasitinib 15 mg, 30 mg ve plasebo
- 1 haftada semptomlarda ve kaşıntıda belirgin azalma
- EASI75

Efficacy and Safety of Upadacitinib in Patients With Moderate to Severe Atopic Dermatitis: Analysis of Follow-up Data From the Measure Up 1 and Measure Up 2 Randomized Clinical Trials

Eric L Simpson [1], Kim A Papp [2], Andrew Blauvelt [3], Chia-Yu Chu [4], H Chih-Ho Hong [5 6 7], Norito Katoh [8], Brian M Calimlim [9], Jacob P Thyssen [10], Albert S Chiou [11], Robert Bissonnette [12], Linda F Stein Gold [13], Colleen Wegzyn [9], Xiaofei Hu [9], Meng Liu [9], John Liu [9], Allan R Tenorio [9], Alvina D Chu [9], Emma Guttman-Yassky [14]



- Neredeyse hastaların yarısı RINVOQ 30 mg ile 2. haftada EASI 75 skoruna ulaşmıştır
- Her iki RINVOQ grubundaki hastaların %60–80'i 16. haftada EASI 75 skoruna ulaşmıştır

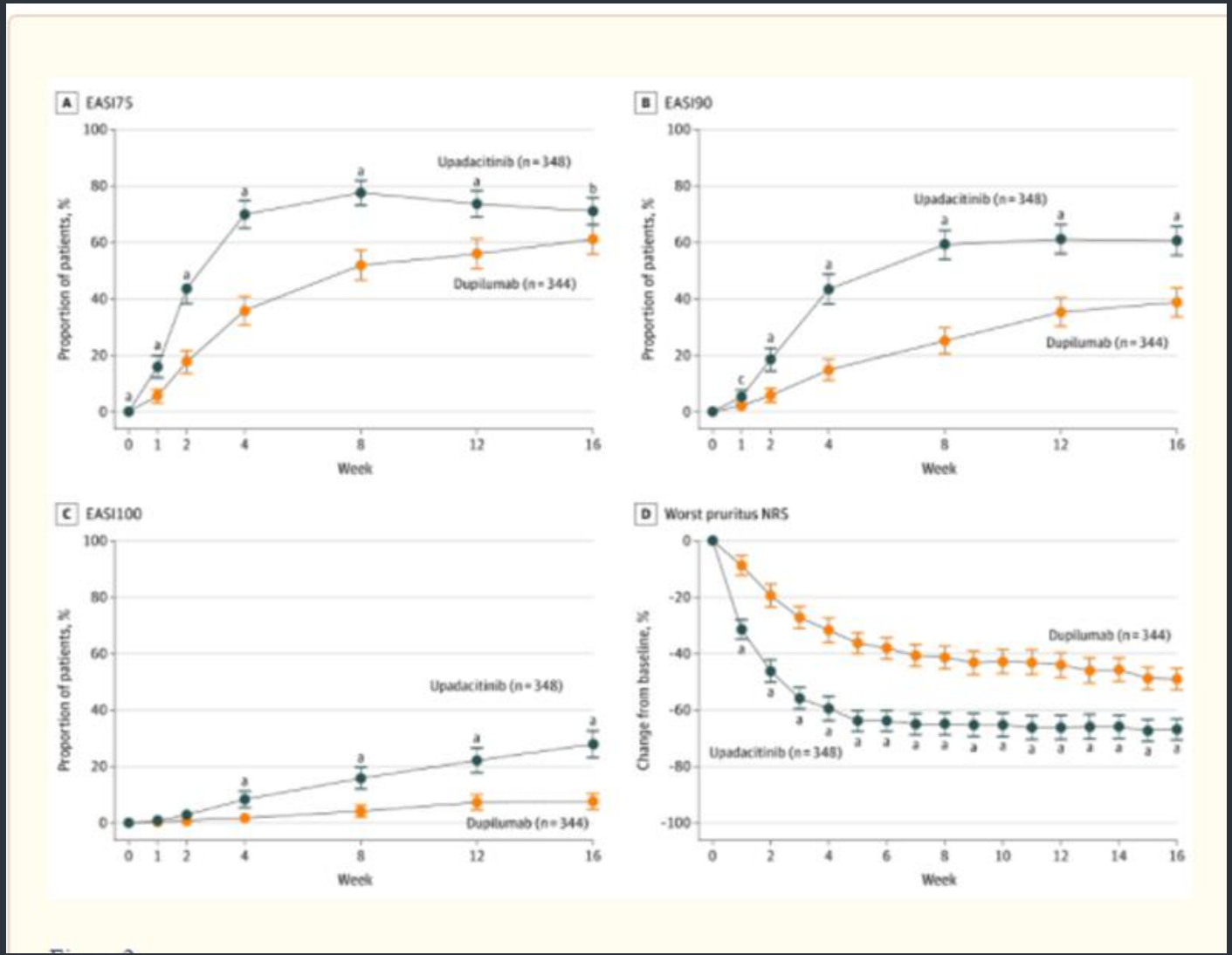
Upadasitinib

Efficacy and Safety of Upadacitinib vs Dupilumab in Adults With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial

Andrew Blauvelt [1], Henrique D Teixeira [2], Eric L Simpson [3], Antonio Costanzo [4 5], Marjolein De Bruin-Weller [6], Sebastien Barbarot [7], Vimal H Prajapati [8 9 10 11 12 13], Peter Lio [14 15], Xiaofei Hu [2], Tianshuang Wu [2], John Liu [2], Barry Ladizinski [2], Alvina D Chu [2], Kilian Eyerich [16 17]

- Upadasitinib **X** Dupilumab
- Dupilumab 300 mg alan 344
- Upadasitinib 30 mg alan 348 hasta
- Gruplar demografik olarak benzer

- 16. haftada EASI75'e ulaşan hastaların oranı, upadasitinib alan hastalarda dupilumab alanlara göre anlamlı olarak daha yüksek
- Upadasitinib için **etki başlangıcı daha hızlı**
- **2. haftada** EASI75'e ulaşan hastaların oranı, dupilumab alanlara kıyasla upadasitinib alan hastalarda anlamlı derecede daha yüksek



Upadasitinib

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester [1], Stanley B Cohen [2], Kevin L Winthrop [3], Peter Nash [4], Alan D Irvine [5] [6], Atul Deodhar [3], Eduardo Mysler [7], Yoshiya Tanaka [8], John Liu [9], Ana P Lacerda [9], Hannah Palac [9], Tim Shaw [10], Philip J Mease [11], Emma Guttman-Yassky [12]

- RA, PsA, AS ve AD tedavisi için upadasitinib 15 mg ve upadasitinib 30 mg (yalnızca AD) klinik çalışmalarından elde edilen güvenlik verileri
- 12 upadasitinib klinik çalışması
- Bazı RA ve PsA çalışmaları, aktif karşılaştırıcılar olarak adalimumab ve metotreksatı içermiştir

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester [1], Stanley B Cohen [2], Kevin L Winthrop [3], Peter Nash [4], Alan D Irvine [5 6], Atul Deodhar [3], Eduardo Mysler [7], Yoshiya Tanaka [8], John Liu [9], Ana P Lacerda [9], Hannah Palac [9], Tim Shaw [10], Philip J Mease [11], Emma Guttman-Yassky [12]

- Toplam **6991** hasta (2693'ü AD)
- Maksimum 5.45 yıl
- AD hastalarında en sık yan etki **AKNE**
- Herpes zoster, NMSC ve CPK'da yükselme
- MACE ve VTE sadece RA grubunda (en az 1 kardiyovask ve tromboembolik risk fakt +)
- Anemi, nötropeni ve lenfopeni gibi yan etkiler RA, PsA, AS ve AD'de bildirildi, çoğunda geçiciydi ve ilacın kesilmesine gerek duyulmadı

Abrositinib

- Seçici JAK1 inhibitörü
- Faz 3 çalışmaları:
- JADE MONO1 ve 2 >12 yaş üstü hastalarda 100 mg/200 mg abrositinib, plasebo ile karşılaştırması
- IGA 0/1 ve EASI75 yanıtları 2. haftada- 12. haftaya kadar da artarak devam etmiş
- Kaşıntıda azalma **2. günde** başlamış

Clinical Trial > Lancet. 2020 Jul 25;396(10246):255-266. doi: 10.1016/S0140-6736(20)30732-7.

Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial

Eric L Simpson [1], Rodney Sinclair [2], Seth Forman [3], Andreas Wollenberg [4], Roland Aschoff [5], Michael Cork [6], Thomas Bieber [7], Jacob P Thyssen [8], Gil Yosipovitch [9], Carsten Flohr [10], Nina Magnolo [11], Catherine Maari [12], Claire Feeney [13], Pinaki Biswas [14], Svitlana Tatulych [15], Hernan Valdez [14], Ricardo Rojo [16]

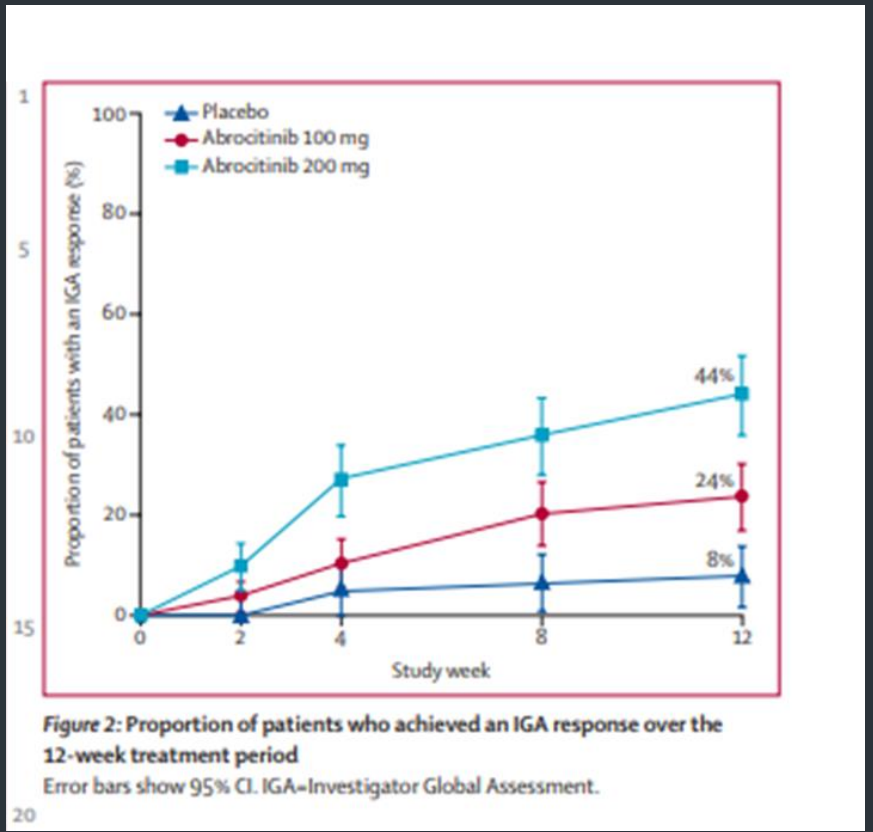


Figure 2: **Proportion of patients who achieved an IGA response over the 12-week treatment period**

Error bars show 95% CI. IGA=Investigator Global Assessment.

Abrositinib

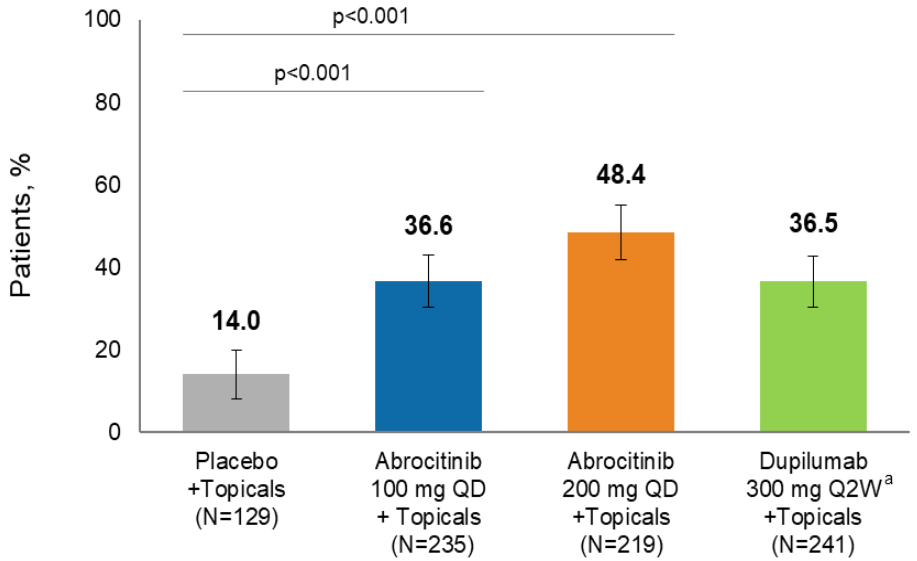
- JADE COMPARE:
- >18 yaş üstü hastalarda 100mg/200 mg abrositinib, plasebo ve dupilumab yanıtlarının karşılaştırılması
- 16 hafta
- 837 hasta

Clinical Trial > J Eur Acad Dermatol Venereol. 2022 Mar;36(3):434-443. doi: 10.1111/jdv.17813. Epub 2021 Dec 13.

Patient-reported outcomes from the JADE COMPARE randomized phase 3 study of abrocitinib in adults with moderate-to-severe atopic dermatitis

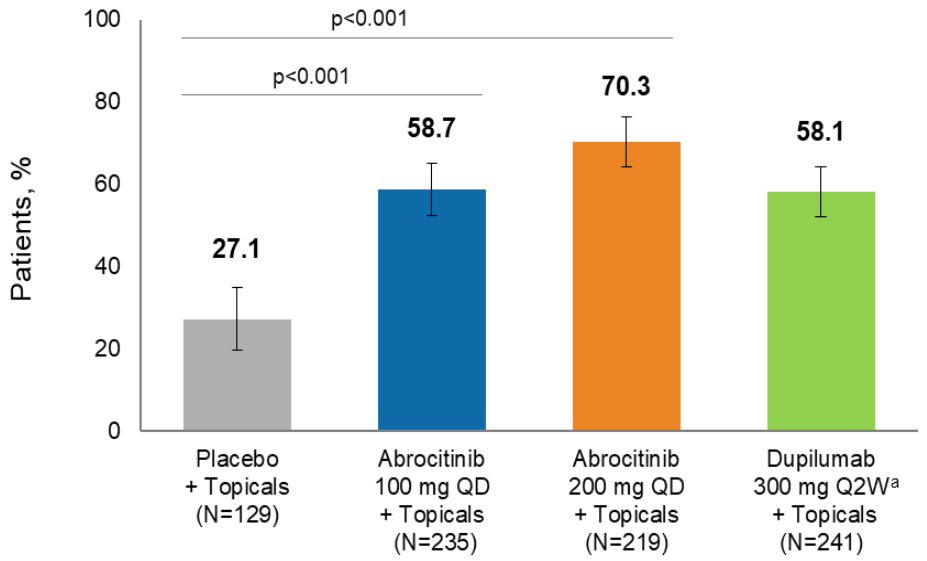
J P Thyssen [1], G Yosipovitch [2], C Paul [3], S G Kwatra [4], C-Y Chu [5], M DiBonaventura [6], C Feeney [7], F Zhang [8], D Myers [9], R Rojo [8], H Valdez [6]

IGA Yanıtına Ulaşanlar



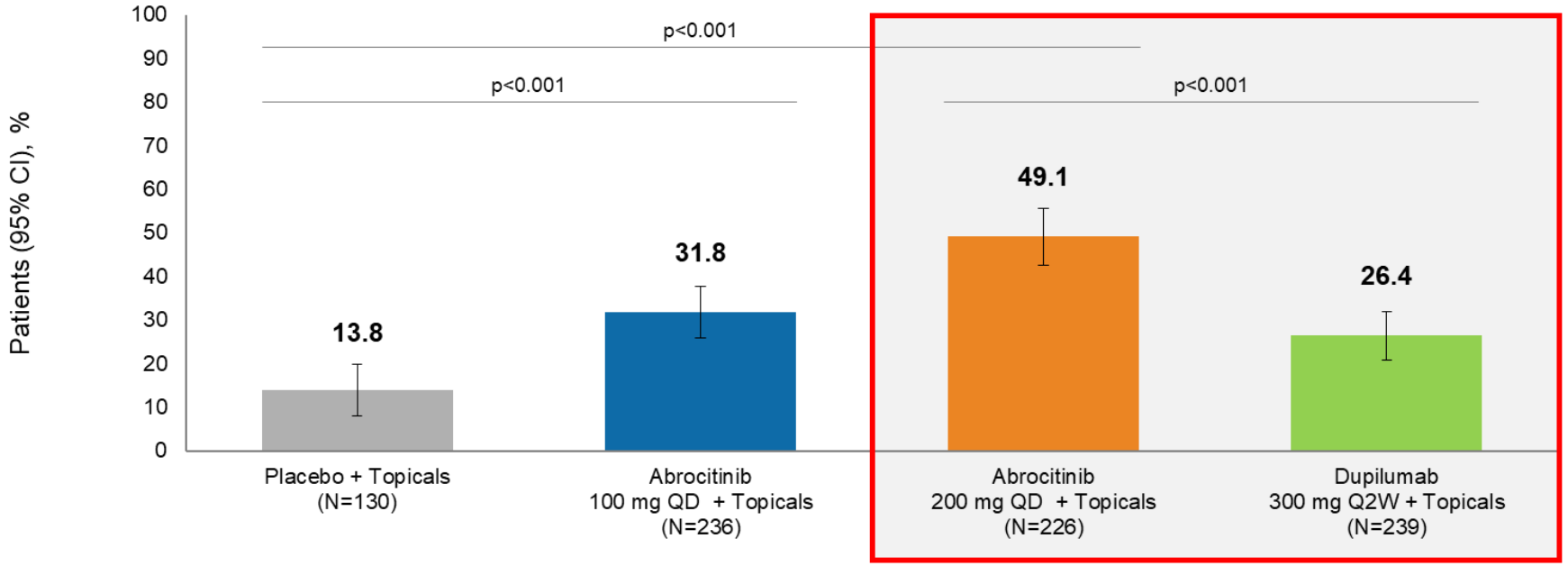
Proportion with IGA clear (0) or almost clear (1) and ≥2-point improvement from baseline at Week 12

EASI-75 Yanıtına Ulaşanlar



Proportion with ≥75% improvement in EASI score from baseline at Week 12

2. Haftada PP-NRS4 Kaşıntı Yanıtına Ulaşanlar



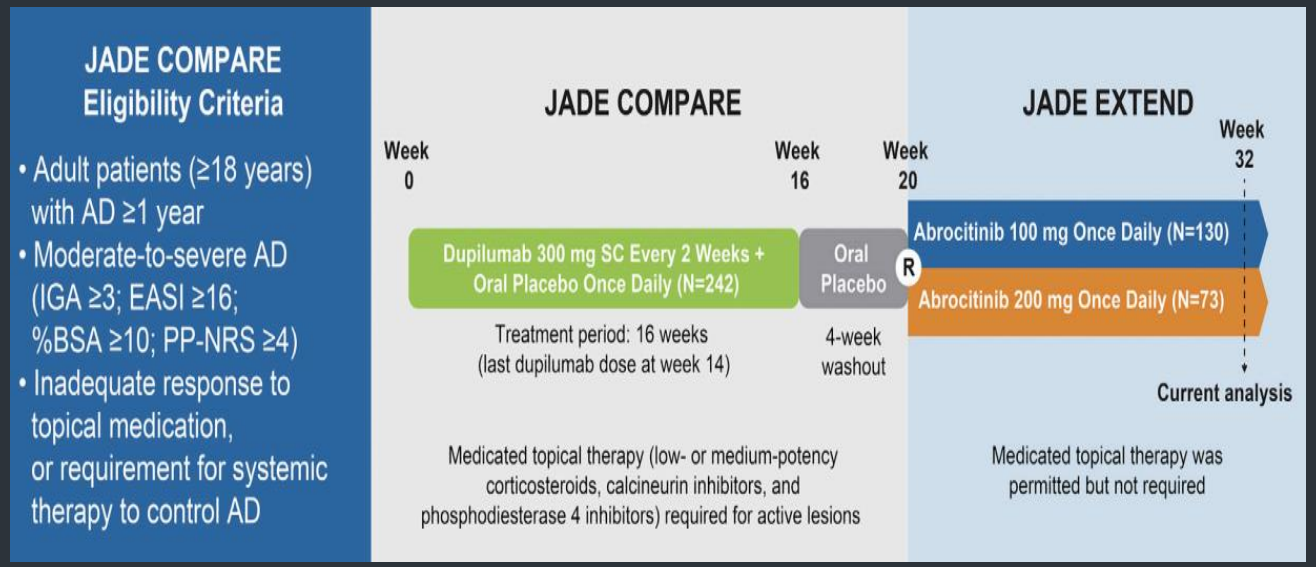
Proportion of patients achieving ≥4-point improvement in the PP-NRS from baseline (abrocitinib vs. dupilumab and abrocitinib vs. placebo) at Week 2

Abrositinib

Clinical Trial > J Am Acad Dermatol. 2022 Aug;87(2):351-358. doi: 10.1016/j.jaad.2022.04.009. Epub 2022 Apr 16.

Phase 3 efficacy and safety of abrocitinib in adults with moderate-to-severe atopic dermatitis after switching from dupilumab (JADE EXTEND)

Vivian Y Shi [1], Tina Bhutani [2], Luz Fonacier [3], Mette Deleuran [4], Stephen Shumack [5], Hernan Valdez [6], Fan Zhang [7], Gary L Chan [8], Michael C Cameron [6], Natalie C Yin [6]



Abrositinib

- En sık yan etkiler
  - Nazofarenjit, mide bulantısı, akne, baş ağrısı
- 1 hastada egzama herpetikum
- 1 hastada trombositopeni

Table IV. Safety summary

	Abrocitinib 100 mg once daily (N = 130)	Abrocitinib 200 mg once daily (N = 73)
Patients with ≥1 treatment-emergent adverse event, n (%)	54 (41.5)	37 (50.7)
Serious adverse events*	3 (2.3)	1 (1.4)
Severe adverse events†	3 (2.3)	2 (2.7)
Adverse events leading to study discontinuation‡	1 (0.8)	1 (1.4)
Treatment-emergent adverse events reported for ≥4 patients in any group, n (%)		
Nasopharyngitis	9 (6.9)	8 (11.0)
Nausea	0	6 (8.2)
Acne	3 (2.3)	5 (6.8)
Headache	1 (0.8)	5 (6.8)
Upper respiratory tract infection	6 (4.6)	2 (2.7)
Urinary tract infection	4 (3.1)	1 (1.4)

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DOI: 10.1111/dth.15636

REVIEW ARTICLE

DERMATOLOGIC THERAPY WILEY

Comparative efficacy and safety of abrocitinib, baricitinib, and upadacitinib for moderate-to-severe atopic dermatitis: A network meta-analysis

Huiying Wan[1] | Haiping Jia[2] | Tian Xia[3] | Dingding Zhang[4]

- Metaanaliz çalışması
- 10 çalışma
- IGA, EASI-75 ve TEAEs plasebo ile kıyaslanıyor
- 12-16 hafta

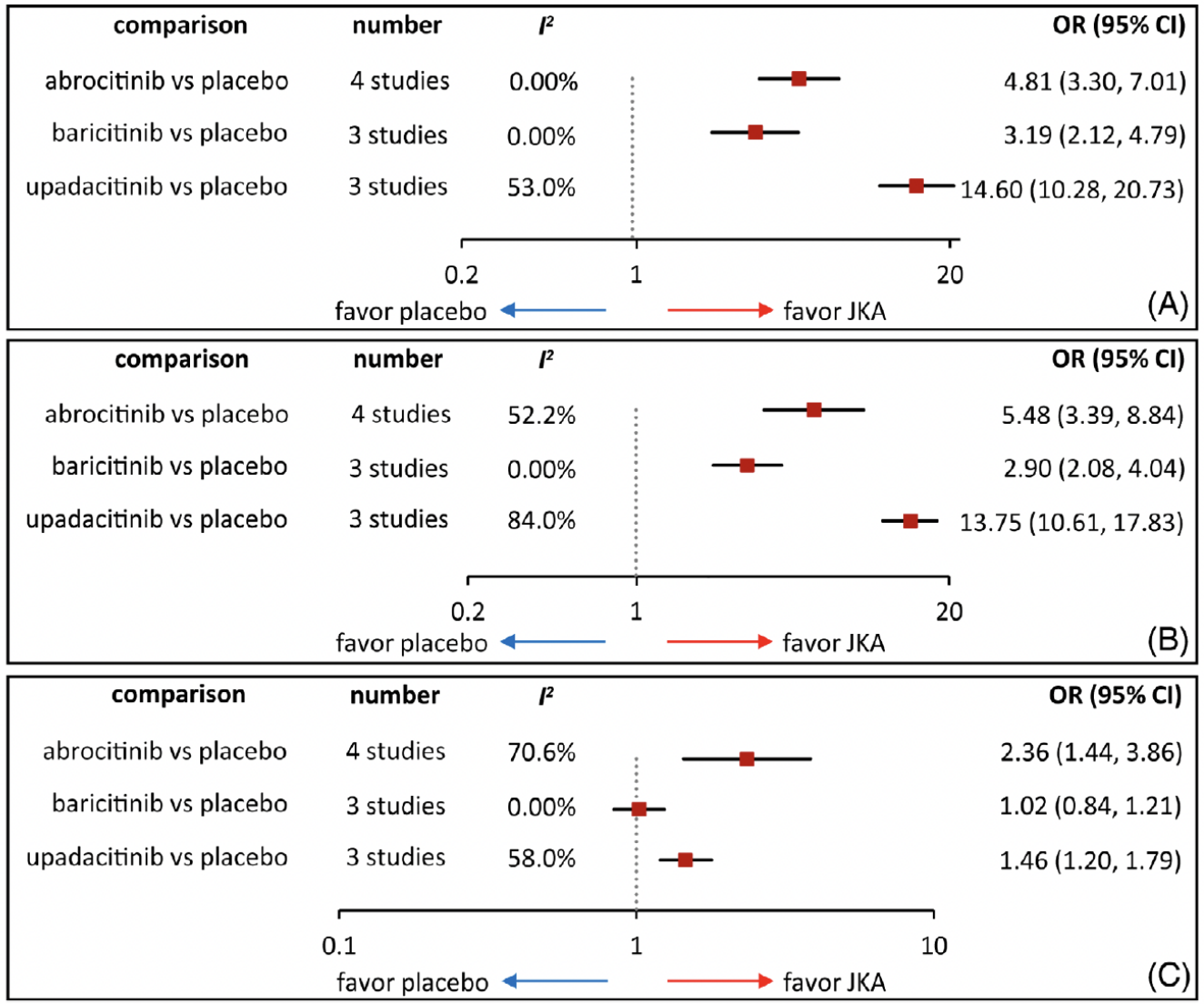

FIGURE 2 Pair-wise meta-analysis of IGA (A), EASI (B), and TEAEs (C). Gray dashed line indicates no statistical significance. Red square represents a point estimate, and black horizontal line represents 95% confidence interval.

Review > Int J Dermatol. 2022 Jun;61(6):746-754. doi: 10.1111/ijd.15853. Epub 2021 Aug 22.

Safety of Janus kinase (JAK) inhibitors in the short-term treatment of atopic dermatitis

Hannah Wood [1 2], Antoinette Chandler [1 2], Novin Nezamololama [2], Kim Papp [3], Melinda J Gooderham [3 4]

- En sık (%2-5) yan etkiler
  - Bulantı
  - ÜSYE
  - Baş ağrısı
  - Akne
  - HSV, herpes zoster
  - CPK'da yükselme

Table 2 Summary of adverse events in the short-term use of systemic JAK inhibitors for atopic dermatitis. Data reported in ranges as percentages unless otherwise noted

	Abrocitinib			Baricitinib				Upadacitinib		
	PBO	100 mg	200 mg	PBO	1 mg	2 mg	4 mg	PBO	15 mg	30 mg
No. of patients (N)	211	370	364	601	251	355	359	902	899	906
	%	%	%	%	%	%	%	%	%	%
All AEs	54–57	63–69	66–78	38–56	53–54	46–58	54-58	53–63	60–76	61–79
SAEs	1.3–4	3–5.4	1.3–3.6	0-4	0.8–7.3	0–2.4	0.8–4	2.5–3	1.8–2.4	0–3
Serious infection	1.3	1.9	0	2	NR	NR	NR	0–1	0.4–2.4	0.7–1
VTE	0	0	0–1.8	0	0	0	1	0–0.4	0	0
Malignancy	0	0	0	0.4	0	0	0	0	0	0–1
Herpes simplex	1.8	0–1.8	0–2	0–4.5	4.8–5.5	0–5.7	4–7	1.7	3.3	7.7
Herpes zoster	0	0–1	0–1.3	0–1*	0*	0-2*	0*	0-1	0-2.2	1–2.1
Death	0	0–0.6	0	0	0	0	0	0	0	0
URTI	4–9	5–9	3–9	2–2.4	1–5	0–7	3	5–10	5–12	5–12
Nasopharyngitis	6–10	13–18	8–13	2–12	11–17	3–13	8.1–15	2.5–11	5–12	5–13
Nausea	2–3	2–9	14–20	NR	NR	NR	NR	2.5	2.4	7.1
Vomiting	0-1.3	0-1.3	0–5.2	NR	NR	NR	NR	NR	NR	NR
Headache	2.6–3.6	5.7–8.9	7.3–10	0–6.4	4.8–5.5	5–11	8–8.9	2.5–5.5	5–7	5–9.5
CPK elevation	0–2.6	0–1.9	0–3.2	0–0.8	0.8–3.2	0.8–3	0–5.7	2.3–5	4–7	5–9.5
Neutropenia	NR	NR	NR	NR	NR	NR	NR	0–1	1–4.8	1–5

*Int J Dermatol. 2022 Jun;61(6):746-754. **Safety of Janus kinase (JAK) inhibitors in the short-term treatment of atopic dermatitis**

Delgositinib

Clinical Trial > J Am Acad Dermatol. 2020 Apr;82(4):823-831. doi: 10.1016/j.jaad.2019.12.015. Epub 2020 Feb 3.

Delgocitinib ointment, a topical Janus kinase inhibitor, in adult patients with moderate to severe atopic dermatitis: A phase 3, randomized, double-blind, vehicle-controlled study and an open-label, long-term extension study

Hidemi Nakagawa [1], Osamu Nemoto [2], Atsuyuki Igarashi [3], Hidehisa Saeki [4], Hironobu Kaino [5], Takeshi Nagata [6]

- Delgositinib 0.5% merhemi, Japonya'da erişkin AD hastalarında endikasyon almış
- 2-15 yaş grubu için Faz III çalışması
- 56 haftaya kadar
- Hafif orta şiddetli AD'de etkili bulunmuş

Ruksolitinib

Randomized Controlled Trial > J Am Acad Dermatol. 2021 Oct;85(4):863-872.
doi: 10.1016/j.jaad.2021.04.085. Epub 2021 May 4.

Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: Results from 2 phase 3, randomized, double-blind studies

Kim Papp [1], Jacek C Szepietowski [2], Leon Kircik [3], Darryl Toth [4], Lawrence F Eichenfield [5], Donald Y M Leung [6], Seth B Forman [7], May E Venturanza [8], Kang Sun [8], Michael E Kuligowski [8], Eric L Simpson [9]

- Topikal selektif JAK 1 ve 2 inhibitörü
- 631 hasta TRuE AD1- 618 hasta TRuE AD2
- % 0,75 ve %1,5 ruksolitinib krem 2*1- 8 hafta
- Uygulama bölgesinde yanma, kaşıntı nadir <%1
- Uyku ve kaşıntı skorlarında anlamlı düzelme

- TEŞEKKÜR EDERİM….