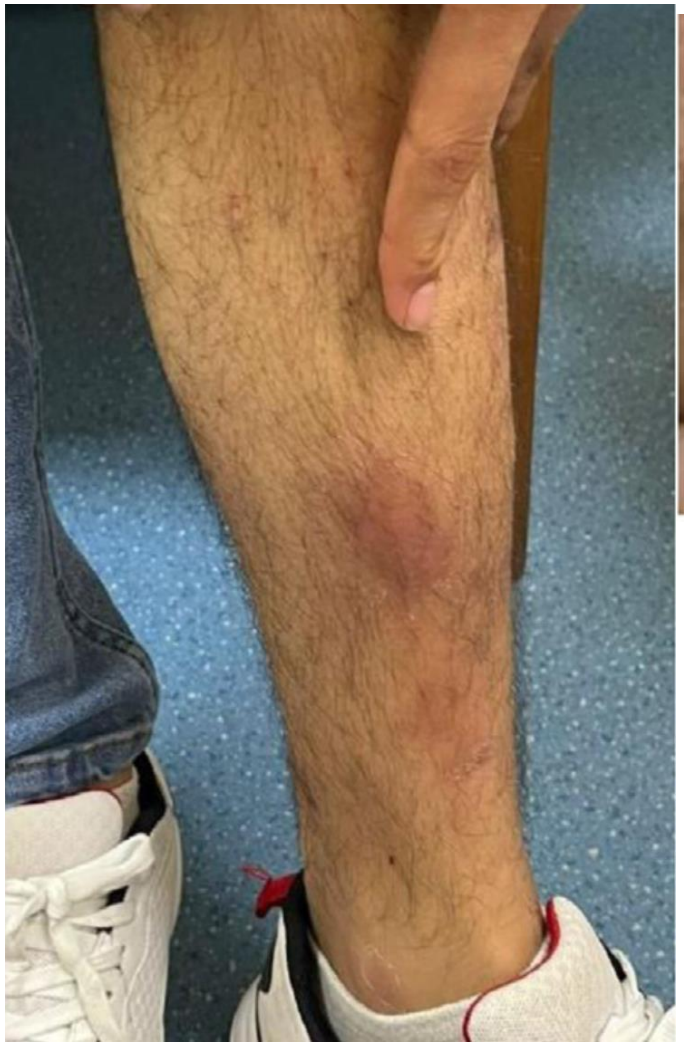
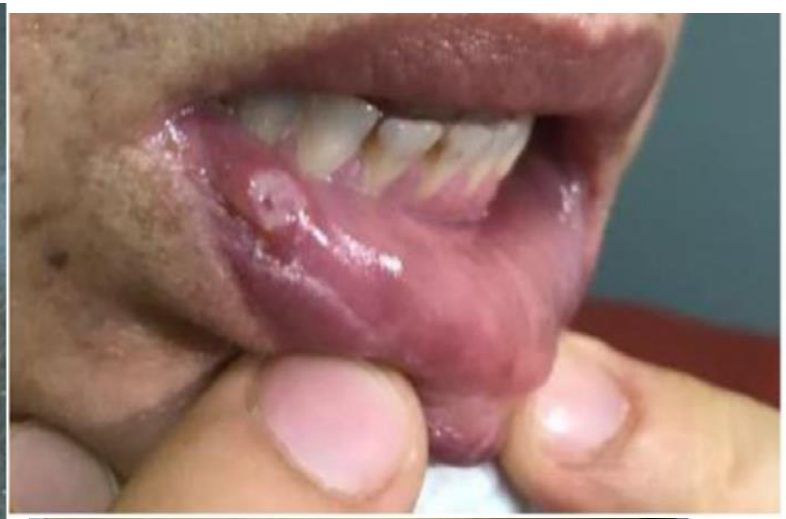
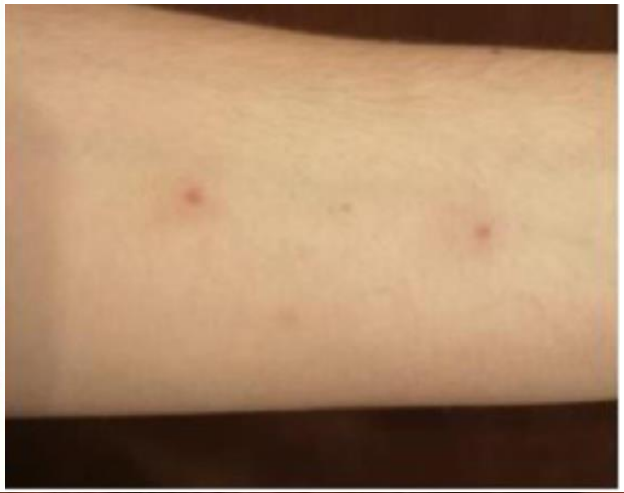
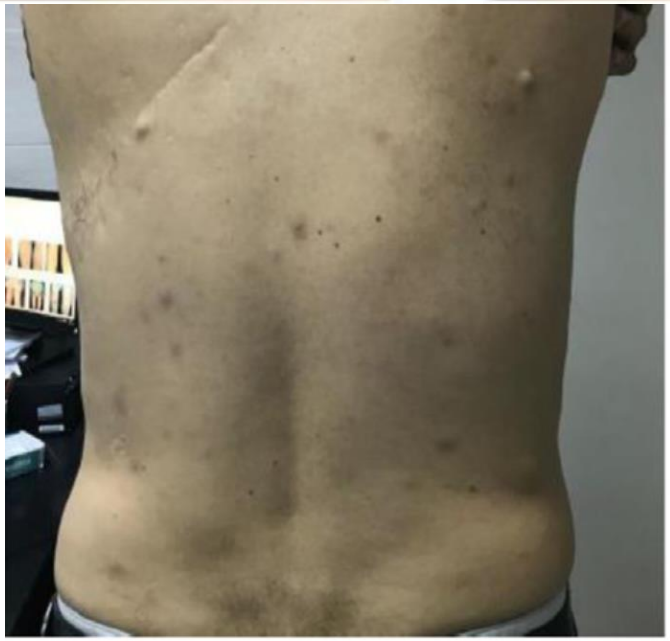
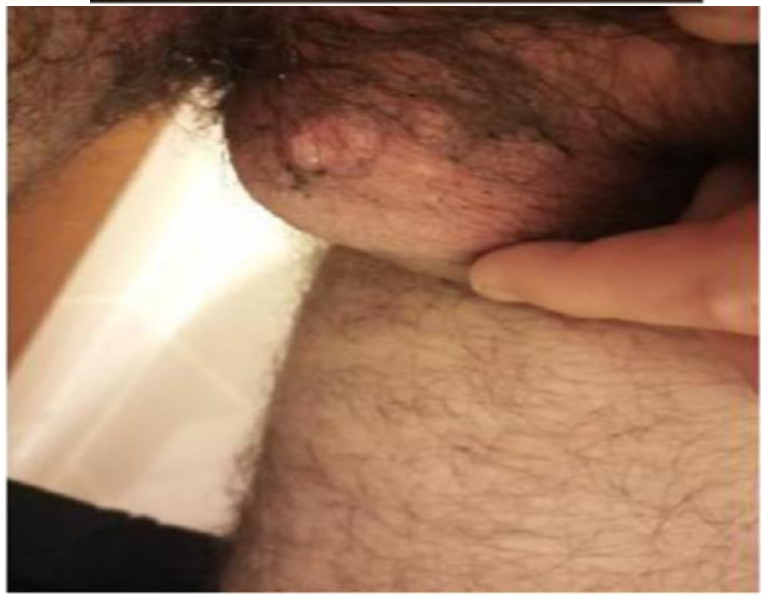
Mukokutanöz Tutulum ve Paterji Reaksiyonu











Figen Tarhan

Recurrent oral ulceration	Minor aphthous, major aphthous, or herpetiform ulceration observed by physician or patient, which recurred at least 3 times in one 12-month period
Plus 2 of:	
Recurrent genital ulceration	Aphthous ulceration or scarring, observed by physician or patient
Eye lesions	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; *or* Retinal vasculitis observed by ophthalmologist
Skin lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis, or papulopustular lesions; *or* Acneiform nodules observed by physician in postadolescent patients not on corticosteroid treatment
Positive pathergy test	Read by physician at 24–48 h.

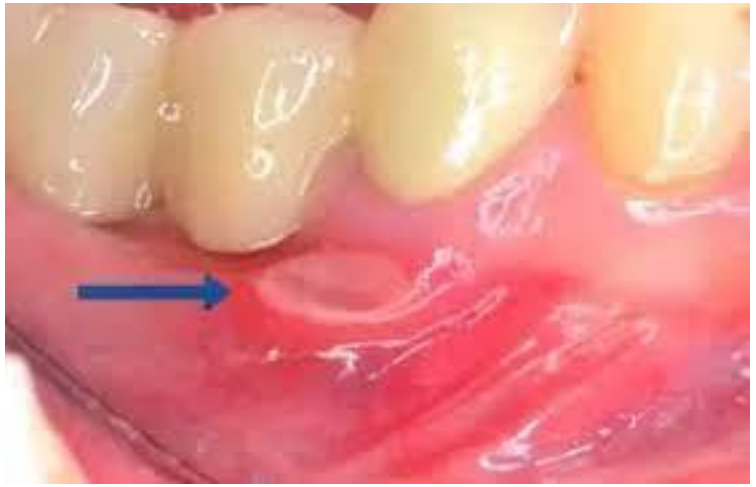
Main points
- Main symptoms
  - Recurrent aphthous ulcers on oral mucosa
  - Skin lesions
    - a. Skin lesion with erythema nodosum
    - b. Subcutaneous thrombophlebitis
    - c. Follicular papules, acneform papules
      cf.) Skin hypersensitivity
  - Ocular lesions
    - a. Iridocyclitis
    - b. Posterior-uveitis (retinochoroiditis)
    - c. If the patients have the following eye symptoms after (a) and (b), diagnose as BD lesions in accordance with (a) and (b)
      Posterior adhesion of iris, pigmentation on lens, retinochoroid atrophy, atrophy of optic nerve, complicated cataract, secondary glaucoma, leakage of bulbus oculi
  - Genital ulcers
- Additional symptoms
  - Arthritis without deformity or sclerosis
  - Epididymitis
  - Gastrointestinal lesion represented by ileocecal ulceration
  - Vascular lesions
  - Central nervous system lesions moderate or severe

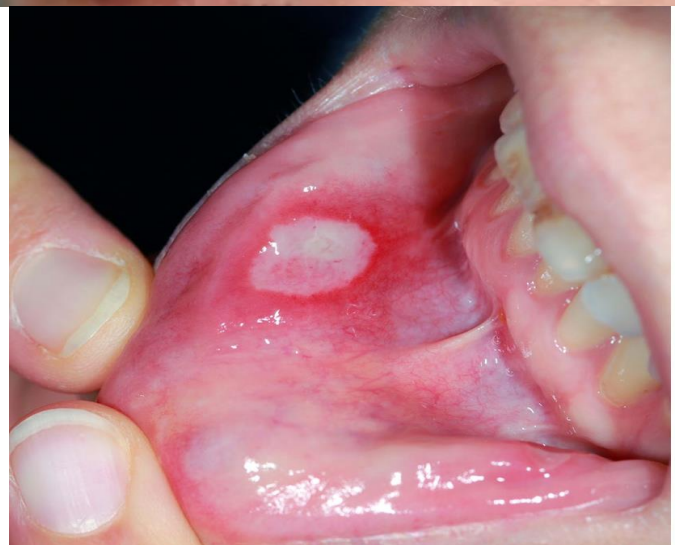
Lancet. 1990 5;335(8697):1078-80

Behcet's Disease (BD) Research Committee of Japan in 2003

- Oral Ülser
- Genital Ülser
- Eritema Nodosum benzeri lezyonlar
- Papülopüstüler lezyonlar
- Yüzeyel tromboflebit
- Diğer Mukokütanöz Lezyonlar
- Paterji reaksiyonu

Oral ülserler





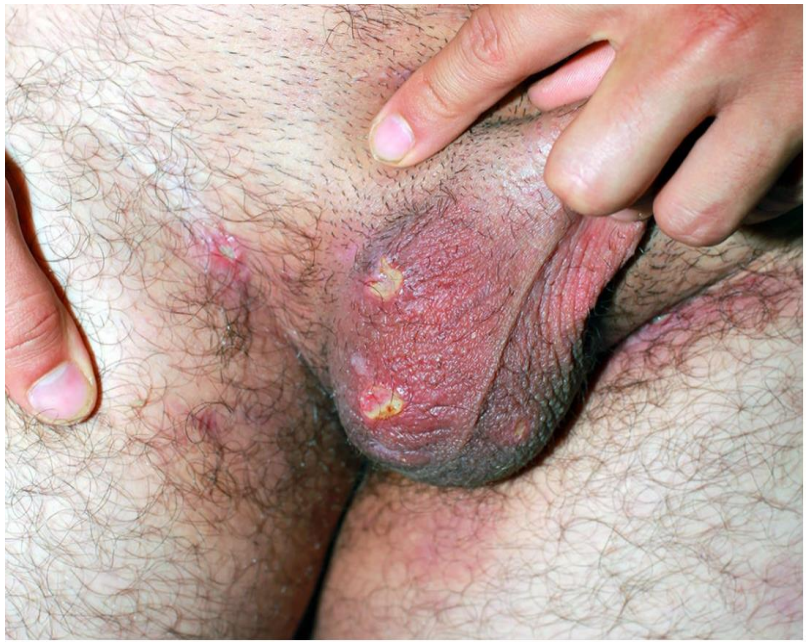
- %92-100
- Minör (%80-85) <1 cm
- Majör(%10-15) >1 cm
- Herpetiform(%5) 1-3 mm boyutunda ve 10-100 adet
- **Dudak bukkal mukoza, diş eti ve dil**, tonsil, farinks
- Histoloji: **nötrofilik perivasküler infiltrasyon , Hem makrofajlar hem de fagositik apoptotik hücreler, hasarlı epitelyal katmanlarda**

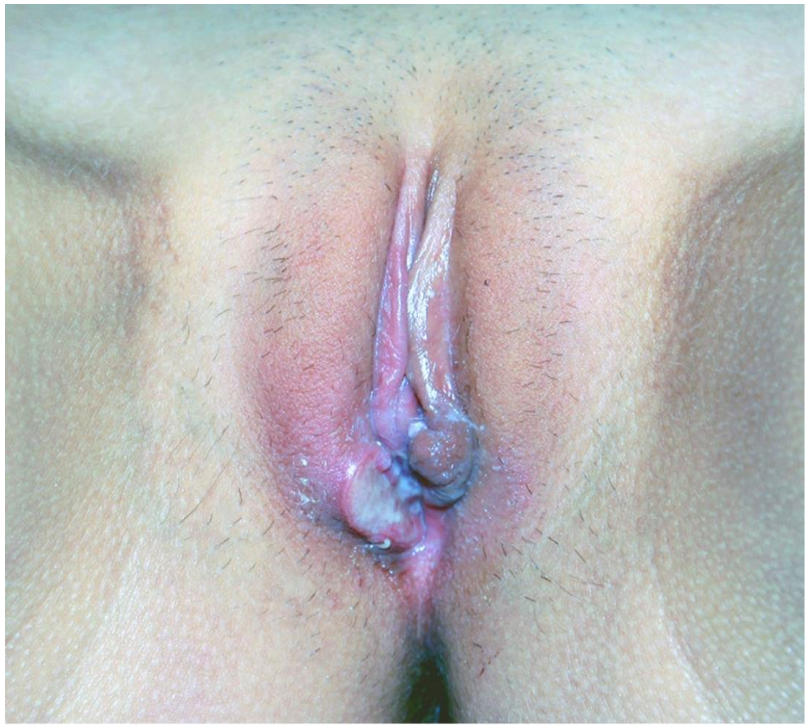
Ayırıcı Tanı

- Herpes Simplex Virüs enfeksiyonu
- Oral eroziv liken planus
- Otoimmün büllöz hastalıklar
- İlaca bağlı mukozal ülserler
- Sistemik Lupus Eritematoz
- Nötropeni
- PFAPA
- MAGIC sendromu
- İnflamatuar Barsak Hastalığı
- HİV
- Reaktif Artrit
- Hiperimmunglobulin D sendromu
- Agranülositoz

Genital Ülser

- %57-93
- Erkekler **skrotum,** penis(korpus, glans), üratra
- Kadın minör **ve majör labia**, vulva, vajina
- Her iki cinsiyette inguinal ve perianal bölge de tutulur

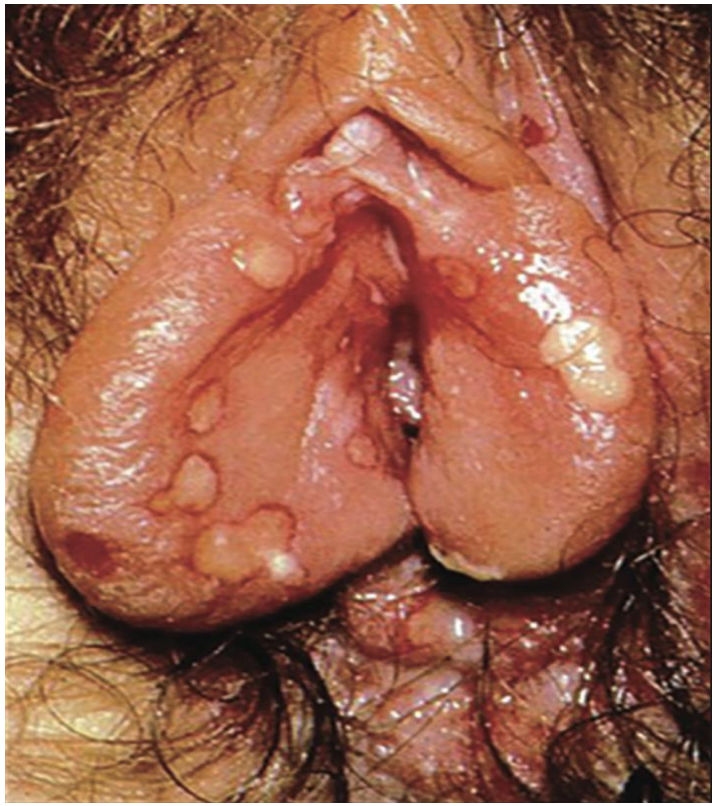


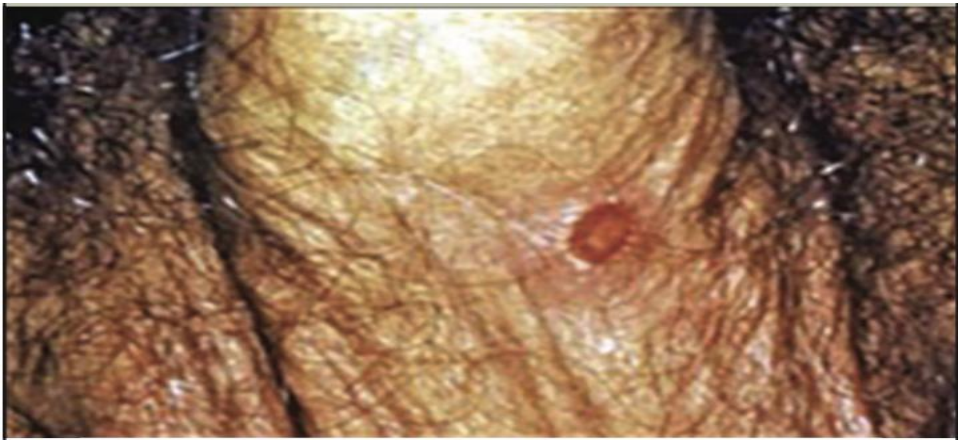


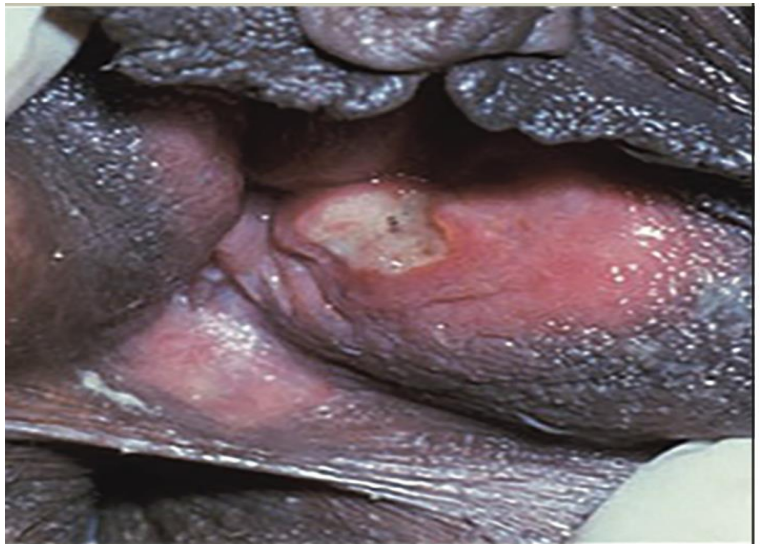
Ayırıcı Tanı

Differential Diagnosis of Genital Ulcers

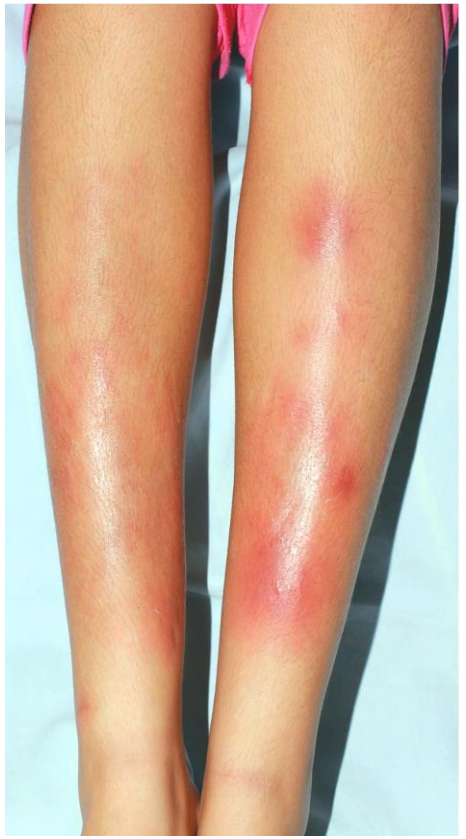
Infectious (most common)*	Noninfectious (less common)
Genital herpes simplex virus	Behçet syndrome
Syphilis	Fixed drug eruption
Chancroid	Psoriasis
Lymphogranuloma venereum	Sexual trauma
Granuloma inguinale (donovanosis)	Wegener granulomatosis
Fungal infection (e.g., Candida)	
Secondary bacterial infection	



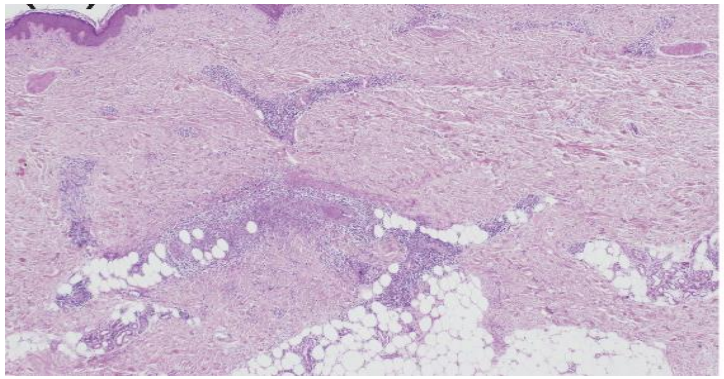


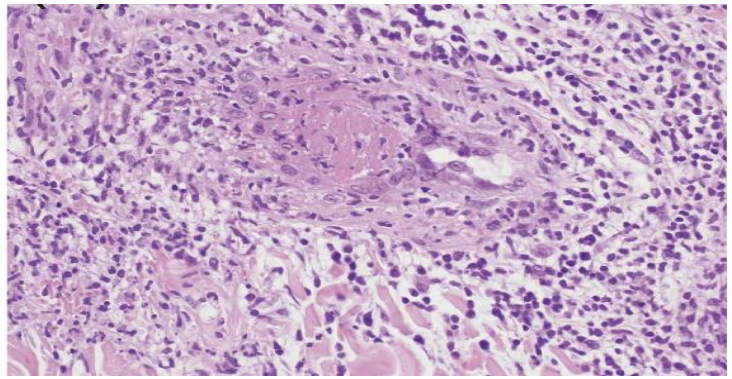


Eritema Nodosum Benzeri Lezyonlar



- %15-75
- Kadınlarda daha sık
- Histoloji:**Çoğunlukla nötrofil olmak üzere lenfositler**
- **kombine olarak infiltrasyon**





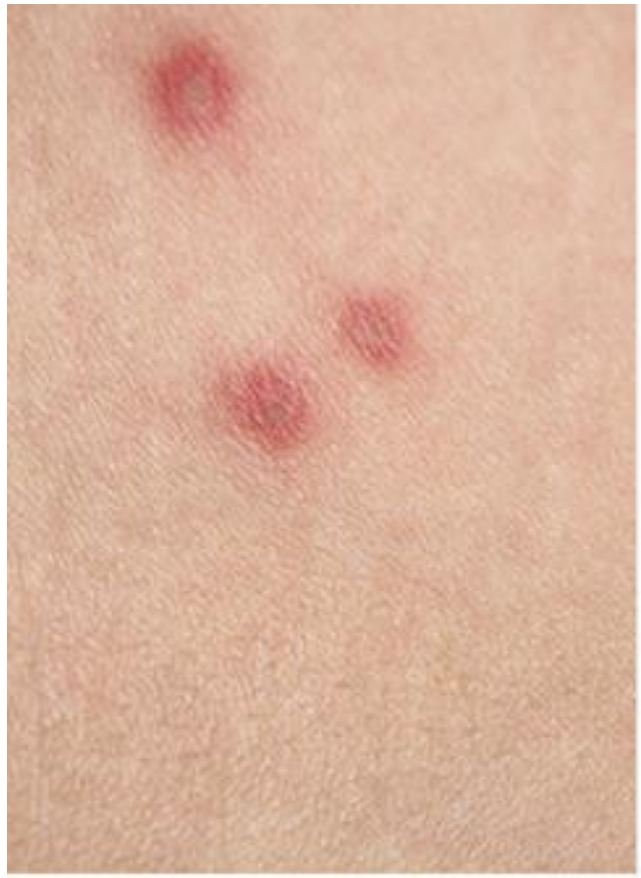
Conditions associated with erythema nodosum

Infections
Bacterial
▪ Streptococcal infection (the most common infectious cause) ▪ Tuberculosis ▪ Leprosy ▪ *Yersinia, Salmonella, Campylobacter* gastroenteritis ▪ *Mycoplasma* pneumonia ▪ Tularemia ▪ Leptospirosis ▪ Brucellosis ▪ *Chlamydia trachomatis* ▪ Psittacosis ▪ Lymphogranuloma venereum ▪ Cat-scratch disease ▪ Q fever (*Coxiella burnetii* infection)
Fungal
▪ Coccidioidomycosis ▪ Histoplasmosis ▪ Blastomycosis
Viral
▪ Infectious mononucleosis ▪ Hepatitis B ▪ Paravaccinia
Drugs
Oral contraceptives
Penicillin
Sulfonamides
Bromides and iodides
TNF-alpha inhibitors (rare)
Inflammatory bowel disease
Crohn's disease (more often than ulcerative colitis)
Ulcerative colitis
Malignancy
Lymphoma (Hodgkin, most often)
Leukemia (acute myelogenous, most often)
Internal carcinomas
Miscellaneous
Sarcoidosis
Pregnancy
Whipple disease
Behçet disease
Sweet syndrome

TNF: tumor necrosis factor.

Papülopüstüler lezyonlar ve Akneiform Erüpsiyonlar

- %65-96
- En sık gövde, alt ekstremite ve yüz
- Histoloji: nötrofilik vaskülit

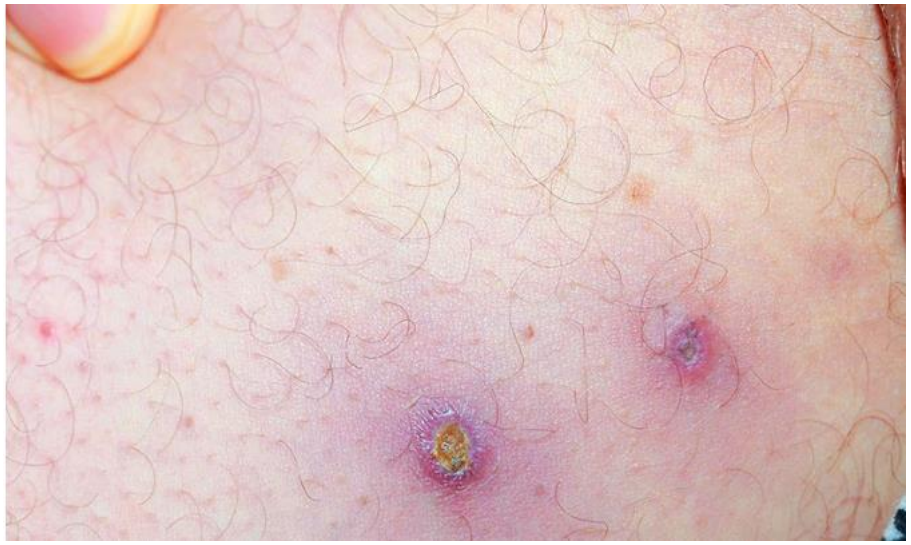


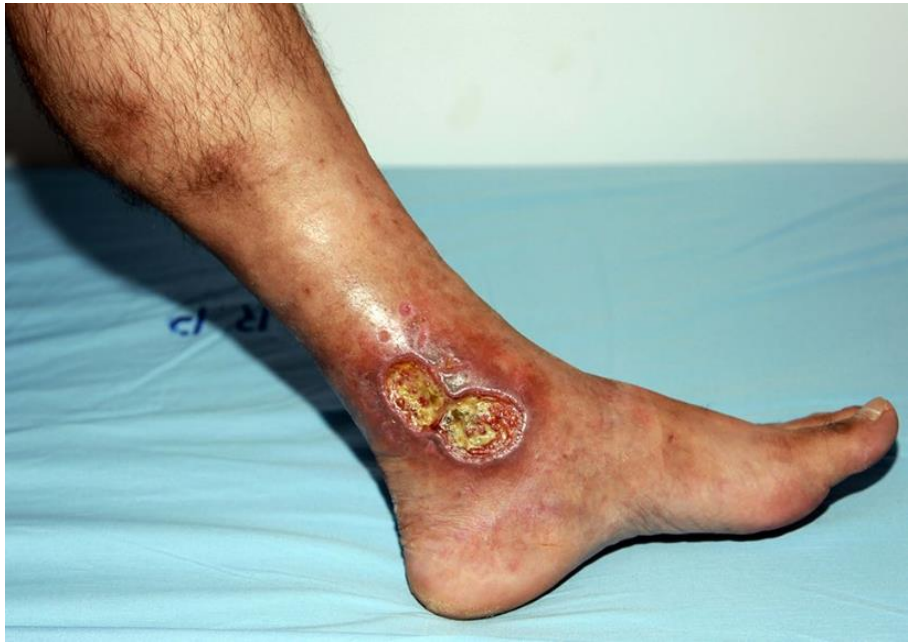
Yüzeyel Tromboflebit

- %10-20
- Erkeklerde daha sık
- Özellikle bacaklarda olmak üzere, damar boyunca hissedilebilen bir sertleşme
- En sık vena saphena magnayı etkiler
- Histoloji: **Yüzeysel subkutan ven lümeninde stenoz ve trombüs oluşumu nötrofil ve lenfositik infiltrasyonları**

Diğer Kutanöz Lezyonlar

- 1- Ekstragenital ülserler(%3)
- 2- Sweet benzeri lezyon(%4)
- Histoloji: deride nötrofilik infiltrasyon gözlenmiştir ve bu nedenle nötrofilik dermatozlar olarak anılırlar.





Nadir Diğer Deri Bulguları

Piyoderma gangrenozum benzeri lezyonlar

Eritema multiforme benzeri lezyonlar

Pernio benzeri kutanöz lezyonlar

Palpabl purpura

Henoch-Schönlein purpurası

Büllöz nekrotizan vaskülit

Subungual enfarktüsler

Hemorajik büller

Fronkül

Apseler

Akral purpurik papülonodüler lezyonlar

Paterji

- Oral
- Subkutan, intravenöz, intradermal

- Lokalizasyon
- Kullanılan iğnenin kalınlığı, iğnenin keskinliği veya küt ucu
- Cildin temizlenmesi
- Delik sayısı

Nasıl Yorumlayalım?

- Eritem
- Papül
- Püstül

- **Pozitif reaksiyonlar, eritematöz papül veya püstüllerin varlığına ve boyutuna bağlı olarak 1+ ila 4+ arasında puanlanır;**

➢ Künt iğnelerle 2 mm ila 3 mm arasında bir papül gözlendiğinde veya keskin iğnelerle 3 mm'ye eşit veya daha küçük bir papül gözlendiğinde 1+

➢ Her iki iğne tipi için de, 3 mm'den büyük herhangi bir papül 2+

➢ 1 mm ila 2 mm arası püstüller 3+ olarak derecelendirilir ve 2 mm'den büyük püstüller 4+ olarak derecelendirilir.

Paterji Testi Pozitiflik Oranları Neden Farklı?

- **Paterji testi uygulama metodolojisi**
- **Etnik özellikler**
- **Yorumlanması**
- **İlaç(KS)**
- **Cinsiyet**

- Orta Doğu, Uzak Doğu ve Akdeniz Havzasını kapsayan İpek Yolu üzerindeki ülkelerde en yüksek
- Türkiye ve İran gibi Doğu Akdeniz bölgesinde %50
- Kore ve Japonya gibi Asya ülkelerinde %30'un altında
- ABD, İngiltere ve diğer Kuzey Avrupa ülkelerinden gelen hastalarda pozitif paterji testleri için rapor edilen oranlar önemli ölçüde daha düşük.

Paterji pozitifliğinin diğer nedenleri

- Piyoderma gangrenozum
- Sweet sendromu
- Eritema elevatum diutinum
- Blind loop syndrome.
- INF alfa tedavisi

Paterji Komplikasyonu

- Paterji yanıtı 48 saatte maksimuma çıkar ve maksimum 45 gün içinde kaybolur
- Abartılı inflamatuar yanıt sonucu doku bütünlüğünün bozulması
- İntraoküler KS sonrası göz enfeksiyonu
- Venipunkturun neden olduğu yüzeysel tromboflebit
- Anjiografi sonrası anevrizma
- Bağırsak rezeksiyonu sonrası anastomoz ülserleri
- Pyöderma gangrenosum rezeksiyonu sonrası ülserlerin katlanarak artması

TEDAVİ

- Tutulan organ
- Organ tutulum aktivitesine
- Hastalık süresi
- Yaş
- Cinsiyet

Kolşisin

Author/year	Number of patients	Outcome	Risk ratio (RR) or mean difference (MD)
Aktulga [2], 1980	28	Improvement in OU score at month 6	RR 0.75 (95% CI 0.48 to 1.17)
		Improvement in GU score at month 6	RR 1 (95% CI 0.37 to 2.70)
		Improvement in PP lesions at month 6	RR 0.07 (%95 CI 0.24 to 1.86)
		Improvement in EN at month 6	RR 2 (95% CI: 0.20 to 19.6)
Yurdakul [3], 2001	116	Number of OU during 2 years (women)	MD −5.73 (95% CI −12.6 to 1.16)
		Number of OU during 2 years (men)	MD 0.80 (95% CI −7.83 to 9.47)
		Number of GU during 2 years (women)	MD −2.50 (95% CI −4.24 to −0.75)
		Number of GU during 2 years (men)	MD −1.10 (95% CI −4.10 to 1.90)
		Number of PP during 2 years (women)	MD −1.80 (95% CI −4.15 to 0.55)
		Number of PP during 2 years (men)	MD 2.60 (95% CI −1.6 5 to 6.85)
		Number of EN during 2 years (women)	MD −4.60 (95% CI −10 to 1.20)
		Number of EN during 2 years (men)	MD −1.30 (95% CI −3.70 to 1.12)
Davatchi [4], 2009	169	IBDDAM score for OU at week 16	MD −0.55 (95% CI −0.99 to 0.10)
		IBDDAM score for GU at week 16	MD −0.22 (95% CI −0.4 to 0.003)
		IBDDAM score for PP at week 16	MD −0.06 (95% CI −0.23 to 0.11)
		IBDDAM score for EN at week 16	MD −0.35 (95% CI −0.57 to −0.12)

The New England
Journal of Medicine

Volume 322 FEBRUARY 1, 1990 Number 5

A CONTROLLED TRIAL OF AZATHIOPRINE IN BEHÇET'S SYNDROME

HASAN YAZICI, M.D., HALIT PAZARLI, M.D., COLIN G. BARNES, M.D., YALÇIN TÜZÜN, M.D., YILMAZ ÖZYAZGAN, M.D., ALAN SILMAN, M.D., SERVER SERDAROĞLU, M.D., VELIEDDIN OĞUZ, M.D., SEBAHATTIN YURDAKUL, M.D., GEORGE E. LOVATT, M.D., BERRIN YAZICI, SHENAZ SOMANI, AND ASUMAN MÜFTÜOĞLU, M.D.

Abstract Cytotoxic agents have long been used in Behçet's syndrome, especially for eye involvement, but their effectiveness has been uncertain. We conducted a two-year randomized, placebo-controlled, double-blind trial of azathioprine (2.5 mg per kilogram of body weight per day) in Turkish men with Behçet's syndrome without eye disease (group 1; n = 25) or with eye disease (group 2; n = 48). Corticosteroid treatment remained available to all the patients.

All six patients withdrawn from the study because of severe eye disease were receiving placebo (P<0.001). Azathioprine was superior to placebo in the prevention of new eye disease in group 1 (1 vs. 8 patients; P<0.01) and in group 2 among the 14 patients who at entry had disease in only one eye (P<0.001). There were fewer episodes of hypopyon uveitis (1 vs. 15; P<0.001) among the group 2 patients who took azathioprine. The patients taking azathioprine also had less frequent oral ulcers, genital ulcers, and arthritis. There were no serious side effects attributable to azathioprine.

We conclude that azathioprine is effective in controlling the progression of Behçet's syndrome, especially its most serious manifestation, eye disease. (N Engl J Med 1990; 322:281-5.)

MANIFESTATION	EVER PRESENT		PRESENT AT INITIAL VISIT		NEW DURING TRIAL*		PRESENT AT 24 MONTHS	
	AZATHIOPRINE (N = 37)	PLACEBO (N = 36)	AZATHIOPRINE (N = 37)	PLACEBO (N = 36)	AZATHIOPRINE	PLACEBO	AZATHIOPRINE (N = 34)	PLACEBO (N = 23)
	number of patients (percent)							
Oral ulceration†	37 (100)	36 (100)	16 (43)	21 (58)	11 (52)	7 (47)	4 (12)	8 (35)
Genital ulceration‡	32 (86)	29 (80)	6 (16)	4 (11)	3 (10)	12 (38)	1 (3)	8 (13)

Thalidomide in the Treatment of the Mucocutaneous Lesions of the Behçet Syndrome

A Randomized, Double-Blind, Placebo-Controlled Trial

Vedat Hamuryudan, MD; Cem Mat, MD; Sebahattin Saip, MD; Yilmaz Özyazgan, MD; Aksel Siva, MD; Sebahattin Yurdakul, MD; Kai Zwingenberger, MD; and Hasan Yazici, MD

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24 haftalık bir RCT
oral ve genital ülserleri ile foliküler lezyonlarının tedavisinde etkilidir

İnterferon-alfa

Author	Year	Duration	Dose	Number of patients (W/M)	Outcome
Hamuryudan [9]	1994	16 weeks	5 MU/3 times per week for 6 weeks 5 MU/week for 10 weeks	20 (12/8)	No significant decrease in the mean number of OU, GU and EN
Azizlerli [8]	1996	12 weeks	3 MU/3 times per week in the first week, 6 MU/3 times per week in the second week, 9 MU/3 times per week in for 14 weeks	18 (13/5)	Reduction in pain, healing time or number of lesions and resolution of at least one symptom ($n=7$) Reduction in pain, healing time or number of lesions ($n=9$) No change ($n=2$)
Alpsoy [11]	1994	8 weeks	3 MU/3 times per week gradually increased to 12 MU/3 times per week	14 (8/6)	Reduction in the frequency of OU, GU and PP No decrease in EN
Boyvat [10]	2000	12 weeks	3 MU/every other day in the first week, 6 MU/every other day in the second week, 9 MU/every other day for 10 weeks	20 (9/11)	Reduction in the frequency and pain of OU, size, pain and duration of GU and number and duration of EN No decrease in PP
O'Duffy [12]	1998	24 weeks	3 MU/day	11 (9/2)	Reduction in the number of OA, GU and cutaneous lesions
Georgiou [13]	1998	8 weeks	6 MU/3 times per week	12 (4/8)	Complete remission ($n=9$) Partial remission ($m=2$) No response ($n=1$)

Short-Term Trial of Etanercept in Behçet's Disease: A Double Blind, Placebo Controlled Study

MELIKE MELIKOGLU, IZZET FRESKO, CEM MAT, YILMAZ OZYAZGAN, FERIDE GOGUS, SEBAHATTIN YURDAKUL, VEDAT HAMURYUDAN, and HASAN YAZICI

ABSTRACT. ***Objective.*** To determine the effect of the tumor necrosis factor-α blocker etanercept on the pathergy and monosodium urate (MSU) status and on the mucocutaneous and articular manifestations of patients with Behçet's disease (BD).

Methods. Forty male patients with BD, all with positive pathergy and MSU tests and mucocutaneous disease and/or arthritis, were randomized (20 patients to each study arm) to receive either etanercept 25 mg twice a week or placebo for 4 weeks. The pathergy and MSU responses and the frequencies of mucocutaneous and articular manifestations were compared between the 2 groups.

Results. There were no decreases in the pathergy and MSU responses in the etanercept group compared to the placebo group at any time. The mean numbers of oral ulcers, nodular lesions, and papulopustular lesions were less in the etanercept group compared to the placebo group at all weekly evaluations, except for the second week for papulopustular lesions. The probability of being free of oral ulcers and nodular lesions was also significantly higher in the former group (log-rank chi-square = 9.83, p = 0.0017; log-rank chi-square = 14.17, p = 0.0002, respectively).

Conclusion. Etanercept did not affect the pathergy reaction and the cutaneous response to MSU crystals. However, the drug was effective in suppressing most of the mucocutaneous manifestations of BD. (J Rheumatol 2005;32:98–105)

Anti-TNF Agents for Behçet's Disease: Analysis of Published Data on 369 Patients

Aikaterini Arida, MD, Kalliopi Fragiadaki, MD, Eirini Giavri, MD, and Petros P. Sfikakis, MD

Objective: Off-label use of anti-tumor necrosis factor (TNF) agents for Behçet's disease (BD) is increasing. We evaluated published data on their efficacy and safety for patients with unmet medical needs due to severe disease manifestations, including ocular, gastrointestinal, and central nervous system involvement.

Methods: Peer-reviewed articles on anti-TNF agents for BD appearing in Medline/PubMed through March 2010 were identified using the appropriate indexing terms.

Results: We found 88, 12, and 13 primary articles from 20 countries on infliximab, etanercept, and adalimumab, reporting on 325, 37, and 28 patients, respectively. All patients were inadequately controlled with, or intolerant to, other immunosuppressive regimens, including interferon; 20 patients received more than 1 anti-TNF agent. In the only randomized placebo-controlled trial, 4-week administration of etanercept was effective in suppressing most of the mucocutaneous manifestations. In 16 open prospective studies evaluating the effect of repetitive infliximab injections (174 patients in total, men:women = 3:1, median follow-up = 16.2 months), sustained organ-specific, clinical responses were evident in 90%, 89%, 100%, and 91% of patients with resistant mucocutaneous, ocular, gastrointestinal, and central nervous system involvement, respectively. Combination of infliximab with azathioprine and/or cyclosporine-A appeared superior to monotherapy for sustained ocular remission. However, due to the fact that necessary data were lacking, formal estimation of anti-TNF treatment effect on the disease activity indexes for different organ involvement was not possible.

Conclusions: Although more controlled data are needed, there is enough published experience to suggest that TNF blockade represents an important therapeutic advancement for patients with severe and resistant, or intolerant, to standard immunosuppressive regimens BD.

 Semin Arthritis Rheum 41:61-70

Apremilast

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Apremilast for Behçet's Syndrome — A Phase 2, Placebo-Controlled Study

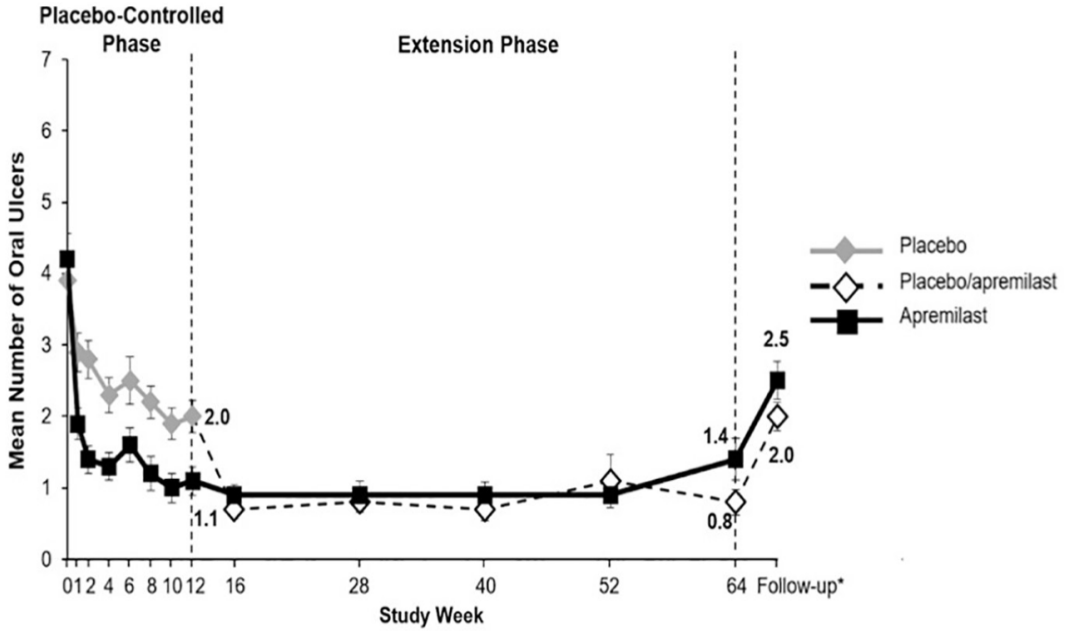
Gulen Hatemi, M.D., Melike Melikoglu, M.D., Recep Tunc, M.D., Cengiz Korkmaz, M.D., Banu Turgut Ozturk, M.D., Cem Mat, M.D., Peter A. Merkel, M.D., Kenneth T. Calamia, M.D., Ziqi Liu, Ph.D., Lilia Pineda, M.D., Randall M. Stevens, M.D., Hasan Yazici, M.D., and Yusuf Yazici, M.D.

- 111 hasta
- Apremilast(60 mgr/gün)&plesebo
- 3 ayda oral ülser pleseboya göre anlamlı düşük
- 3 ayda oral ülser ağrısı apremilast grubunda anlamlı azalma
- Apremilast behçetin oral ülserlerinde etkilidir.

Apremilast for oral ulcers associated with active Behçet's syndrome over 68 weeks: long-term results from a phase 3 randomised clinical trial

G. Hatemi[1], A. Mahr[2], M. Takeno[3], D.Y. Kim[4], D. Saadoun[5], H. Direskeneli[6], M. Melikoğlu[1], S. Cheng[7], S. McCue[7], M. Paris[7], M. Chen[7], Y. Yazici[8]

Clinical and Experimental Rheumatology 2021



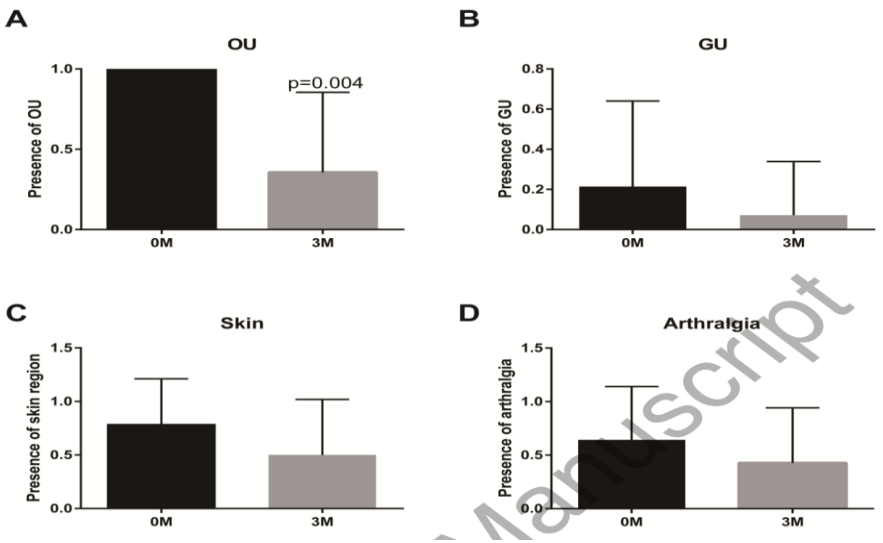
Week	0	1	2	4	6	8	10	12	16	28	40	52	64	Follow-up*
Placebo, n	103	98	97	93	91	86	83	82†						
Placebo/apremilast, n									83	78	73	70	67	82
Apremilast, n	104	101	101	101	98	94	94	97	95	92	85	79	75	85

Modern Rheumatology

ISSN: 1439-7595 (Print) 1439-7609 (Online) Journal homepage: https://www.tandfonline.com/loi/imor20

Efficacy and Safety of Apremilast for 3 Months in Behçet's Disease: A Prospective Observational Study

Lisa Hirahara, Yohei Kirino, Yutaro Soejima, Mitsuhiro Takeno, Kaoru Takase-Minegishi, Ryusuke Yoshimi, Masaki Takeuchi, Nobuhisa Mizuki & Hideaki Nakajima



Clin Rheumatol
DOI 10.1007/s10067-013-2443-8

CASE BASED REVIEW

Anakinra treatment in drug-resistant Behcet's disease: a case series

Luca Cantarini · Antonio Vitale · Perla Scalini · Charles A. Dinarello · Donato Rigante · Rossella Franceschini · Gabriele Simonini · Giulia Borsari · Francesco Caso · Orso Maria Lucherini · Bruno Frediani · Ilaria Bertoldi · Leonardo Punzi · Mauro Galeazzi · Rolando Cimaz

- Standart ve TNFi dirençli hasta
- Tüm hastalarda majör organ tutulumuna ek olarak aktif mukokutanöz lezyonlar da mevcut

Patient	Age	Gender	Age at onset	HLA-B51	ISG criteria	Clinical manifestations	Pathergy test	Follow-up (months)
1	47	M	32	+	+	Bipolar aphthosis, erythema nodosum, retinal vasculitis, headache, hypertension, and recurrent low back pain	–	9
2	21	F	10	+	+	Bipolar aphthosis, erythema nodosum, pseudofolliculitis, arthritis, abdominal pain, and headache	–	19
3	39	M	30	+	+	Bipolar aphthosis, vasculitis, thrombosis headache, papulopustular skin lesions, and recurrent fever	–	19
4	59	F	43	+	+	Bipolar aphthosis, panuveitis, retrobulbar optic neuritis, papillophlebitis, headache, and arthralgia venous thrombosis	–	6
5	29	F	12	+	+	Bipolar aphthosis, uveitis, neurologic involvement	–	8
6	47	M	43	+	+	Bipolar aphthosis, thrombophlebitis, panuveitis, headache, arthritis and recurrent fever	–	12
7	7	M	2	+	+	Bipolar aphthosis, skin ulcers vasculitic rash, abdominal symptoms, and severe photophobia	–	9
8	21	M	20	+	+	Bipolar aphthosis, erythema nodosum, pseudofolliculitis, uveitis, arthritis, recurrent fever, and urogenital symptoms	–	6
9	41	F	33	+	+	Bipolar aphthosis, headache, uveitis, abdominal pain diarrhea, arthralgia, and prolonged fever episodes	–	9

Grayson *et al. Arthritis Research & Therapy* (2017) 19:69
DOI 10.1186/s13075-017-1222-3

Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

Treatment of mucocutaneous manifestations in Behçet's disease with anakinra: a pilot open-label study

Peter C. Grayson[1], Yusuf Yazici[2], Melissa Merideth[1], H. Nida Sen[1], Michael Davis[1], Elaine Novakovich[1], Elizabeth Joyal[1], Raphaela Goldbach-Mansky[1] and Cailin H. Sibley[1,3*]

Patient	Age (years)	Sex	Country of origin	Race	Relevant prior treatment	Current treatment	Historical disease features	Age at ulcer onset (years)	Primary outcome
1	59	F	USA	Caucasian	Abatacept Adalimumab Azathioprine Colchicine Glucocorticoids Infliximab	Azathioprine	**Oral and genital ulcers**, GI ulcers, **skin pustules**, **arthralgias**	7	Treatment failure
2	19	F	USA	Caucasian	Colchicine Glucocorticoids Sulfasalazine	Colchicine Sulfasalazine Prednisone (15 mg/day)	**Oral and genital ulcers**, GI ulcers, thrombophlebitis, **arthralgias, skin pustules**, folliculitis, pathergy, **HLA-B51-positive**	16	Complete response
3	40	F	USA	Mixed	Colchicine, Hydroxychloroquine Glucocorticoids	Colchicine Hydroxychloroquine	**Oral and genital ulcers**, **skin pustules, arthritis**	38	Partial response
4	30	F	USA	Caucasian	Colchicine Glucocorticoids	None	**Oral and genital ulcers, skin pustules**, anterior uveitis, arthritis	2	Complete response
5	26	F	USA	Caucasian	Azathioprine Glucocorticoids	Azathioprine	**Oral and genital ulcers**, GI ulcers, **skin pustules**, deep vein thrombosis	21	Treatment failure
6	36	M	Ethiopia	African	Colchicine Glucocorticoids	Prednisone (20 mg/day)	Oral and genital ulcers, skin pustules, panuveitis, arthritis	31	Partial response

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journal homepage: www.elsevier.com/locate/jautimm

Ustekinumab for Behçet's disease

Adrien Mirouse, M.D. [a, b, c, d], Stéphane Barete, M.D. Ph.D. [a, b, e], Jean-Benoît Monfort, M.D. [f], Matthieu Resche-Rigon, M.D., Ph.D. [g, h], Anne-Sophie Bouyer, M.D. [a, b, c, d], Cloé Comarmond, M.D. Ph.D. [a, b, c, d], Damien Sène, M.D. Ph.D. [i], Fanny Domont, M.D. [a, b, c, d], Yasmina Ferfar, M.D. [a, b, c, d], Patrice Cacoub, M.D. Ph.D. [a, b, c, d, 1], David Saadoun, M.D. Ph.D. [a, b, c, d, *, 1]

- CD dirençli, %70 immünsüpressif kullanmış
- Tam remisyon 3 ay oral ülser yok
- %64,3 tam remisyon, %21,4 kismi remisyon, %14.3 yanıt yok
- 7 ay 10 hasta devam

Main outcome of BD patients treated by ustekinumab.

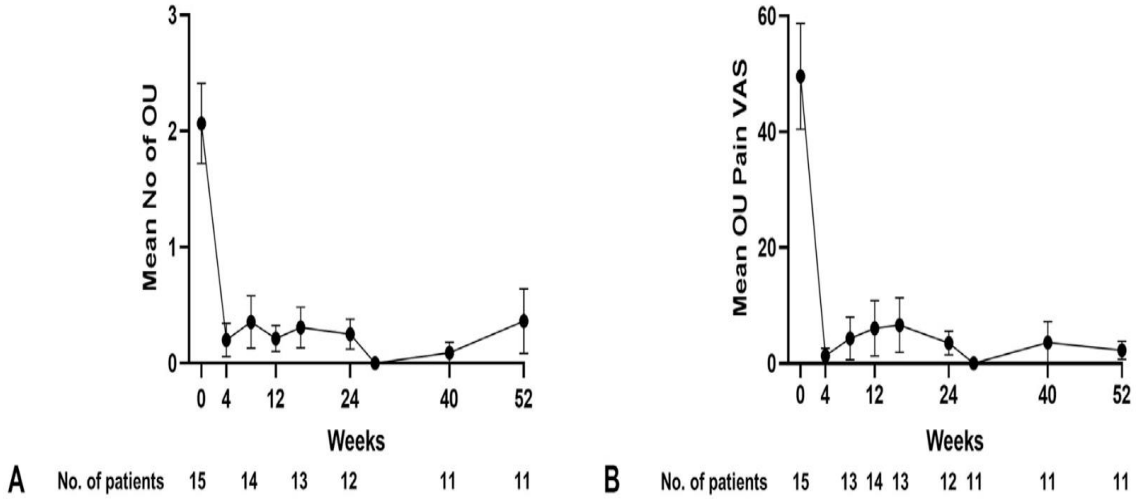
Case	Follow-up (months)	Ustekinumab dose (mg)	Adjunct therapy type (dose, duration prior inclusion)	Steroids dose at baseline/EOF (mg/day)	Steroids and/or adjunct therapy indication	Adverse effects	Outcome of OU at week 12	Relapse during follow-up (month)	Still receiving ustekinumab at the EOF
1	11	90	Steroids (4 years)	20/10	Scleritis	None	CR	Yes, scleritis (8)	No, switch to certolizumab
2	29	45	Steroids (2 years), TCZ (8 mg/kg/ 4weeks, 2 years)	25/5	Pyoderma gangrenosum	None	CR	Yes, Pyoderma gangrenosum (15)	Yes
3	11	90	Steroids (3 years)	10/5	Articular manifestations	None	CR	No	Yes
4	11	90	None	None		Headache	Complete response	No	Yes
5	6	90	None	0/7		Headache	Non responder	No	No, switch to steroids
6	14	90	Steroids (8 months)	15/5		None	Complete response	No	Yes
7	15	90	None	None		None	Partial response	No	No, switch to thalidomide
8	4	90	None	None		None	Complete response	No	Yes
9	7	45	Steroids (1 year), azathioprine (150 mg/day, 6 months)	10/5	Previous CNS involvement	None	Complete response	No	Yes
10	4	90	None	None		Headache	Partial response	No	Yes
11	3	45	Steroids (3 years), azathioprine (100 mg/day, 3 years), colchicine	10/10	GI and articular manifestations	None	Non responder	Yes, pseudo-folliculitis and GI manifestations (2)	No, switch to certolizumab
12	3	90	None	None		None	Complete response	No	Yes
13	3	90	Steroids (4 years), MMF (1 g/day, 3 years)	15/10	Previous CNS involvement	None	Complete response	No	Yes
14	3	90	MMF (3 g/day, 3 years), tacrolimus (3 mg/day, 3 years), steroids (3 years)[a]	5/5	Pyoderma gangrenosum and heart transplant	None	Partial response	Yes, Pyoderma gangrenosum (2)	Yes

J Am Acad Dermatol
Volume 87, Number 3

Efficacy and safety of ustekinumab in Behçet disease: Results from the prospective phase 2 STELABEC trial

J Am Acad Dermatol
September 2022

- CD dirençli
- Son 3 ayda 2 den fazla oral/genital ülser olan
- Komplet Yanıt : 6 ayda oral/Genital ülser yok
- Parsiyel Yanıt: 6 ayda oral/Genital ülser %50 azalma
- 9 hasta tam yanıt, 2 hasta parsiyel yanıt



Tocilizumab

- 21 mukokütanöz
- 4 dirençli
- 9 düzelme, 12 yanıt yok

- Shapiro LS et. al. Clin Neu- rol Neurosurg 114(3):297–298.
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- Diamantopoulos AP et. al. Rheumatology (Oxford) 52(10):1923–1924.
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- Cantarini L. et. al. Clin Rheumatol 34(6):1141–1143
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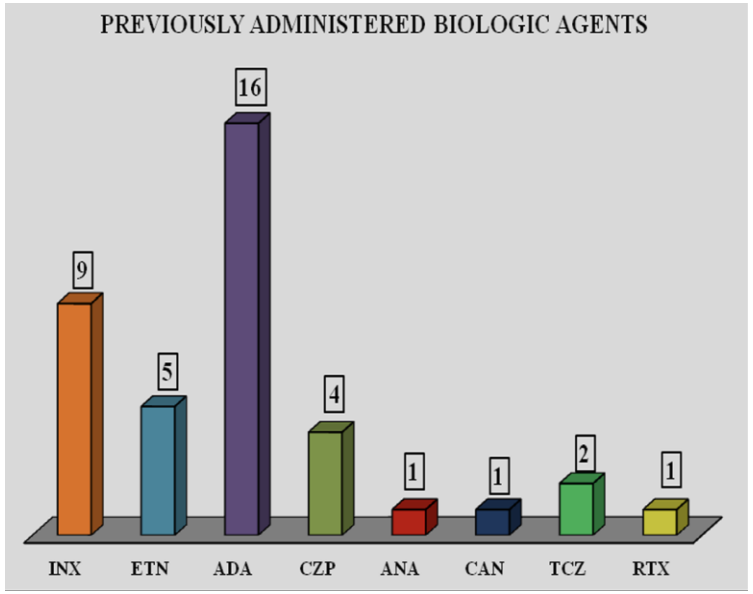
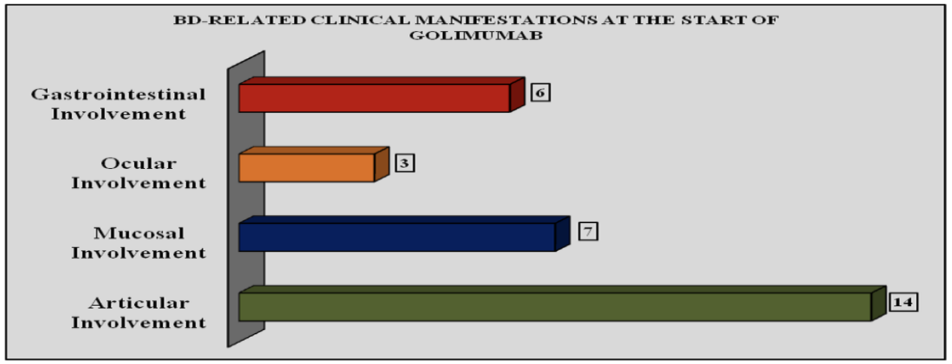
Clin Rheumatol (2017) 36:2063–2069
DOI 10.1007/s10067-017-3627-4

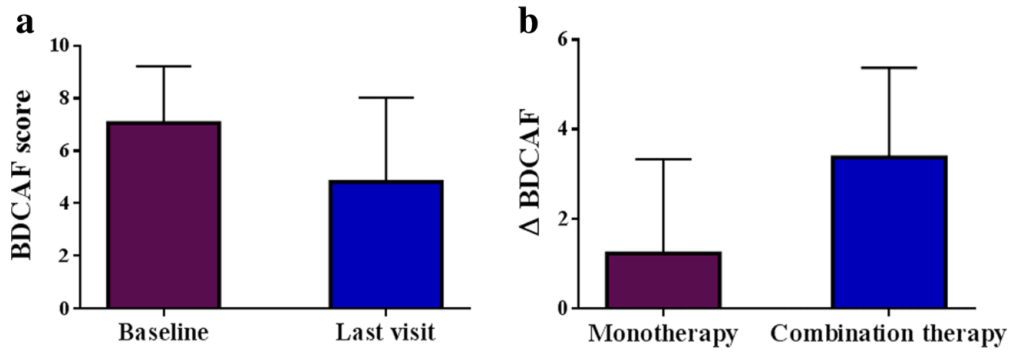
ORIGINAL ARTICLE

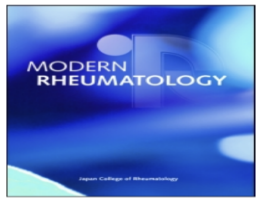
Long-term efficacy and safety of golimumab in the treatment of multirefractory Behçet's disease

Antonio Vitale[1] · Giacomo Emmi[2] · Giuseppe Lopalco[3] · Claudia Fabiani[4] · Stefano Gentileschi[1] · Elena Silvestri[2] · Di Scala Gerardo[2] · Florenzo Iannone[3] · Bruno Frediani[1] · Mauro Galeazzi[1] · Giovanni Lapadula[3] · Donato Rigante[5] · Luca Cantarini[1,6]









Modern Rheumatology

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Certolizumab Pegol treatment in Behcet's disease with different organ involvement: A multicenter retrospective observational study

Giuseppe Lopalco, Giacomo Emmi, Stefano Gentileschi, Silvana Guerriero, Antonio Vitale, Elena Silvestri, Matteo Becatti, Iacopo Cavallo, Claudia Fabiani, Bruno Frediani, Florenzo Iannone & Luca Cantarini

Patient	Duration of CZP therapy (months)	BDCAF at CZP start	BDCAF at last clinical follow-up (if still in treatment) or CZP suspension	Δ-BDCAF	Line of biological therapy (under CZP)	CC associated + PDN variation	DMARDs associated + DMARDs variation	Switch to another biologic drug
1	6	10	7	3	First	MPD 4 mg/day	–	–
2	12	7	5	2	First	PDN 5 mg/day	MMF	–
3	10	7	5	2	Second	MPD 4 mg/day	MTX resumption 7.5 mg/sett	–
4	4	8	9	−1	Second	BDN 800 mg × 3/day	–	IFX 5 mg/kg
5	2	8	10	−2	Second	PDN increased to 10 mg/day	–	IFX 5 mg/kg
6	8	8	7	1	Second	PDN 7.5 mg/day	AZA	–
7	6	7	8	−1	Second	PDN 5 mg/day	MTX	IFX 5 mg/kg
8	5	9	9	0	Second	PDN 5 mg/day	–	GOL 50 mg/month
9	13	10	10	0	Second	PDN 7.5 mg/day	MTX increased to 15 mg/week	–
10	4	8	8	0	Second	PDN 25 mg/day	–	GOL 50 mg/month
11	4	7	10	−3	Third	–	–	GOL 50 mg/month
12	11	11	11	0	Fourth	PDN 7.5 mg/day	AZA increased to 100 mg/day	–
13	5	8	5	3	Sixth	PDN 5 mg/day	SSZ, COL	–

ARTICLE IN PRESS

Journal of Autoimmunity xxx (xxxx) xxx–xxx

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journal homepage: www.elsevier.com/locate/jautimm

Efficacy of the anti-IL 17 secukinumab in refractory Behçet's syndrome: A preliminary study

Gerardo Di Scala[a,1], Alessandra Bettiol[a,b,1], Rafaela Diana Cojan[a], Martina Finocchi[a], Elena Silvestri[a], Giacomo Emmi[a,*]

	Baseline	3 months	6 months	9 months	12 months	15 months
Treatment; achievement of response						
Subject 1	Start Secukinumab 300mg / month + MTX.	Discontinuation of MTX for achievement of complete response	Maintain complete response	Maintain complete response		
Subject 2	Start Secukinumab 150 mg/ month.	No response	Achievement of partial response Switch to Secukinumab 300 mg/ month	Achievement of complete response	Maintain complete response	
Subject 3	Start Secukinumab 150 mg/ month.	No response	Achievement of complete response	Loss of complete response Switch to Secukinumab 300 mg/ month	Re-achievement of complete response	Maintain complete response
Subject 4	Start Secukinumab 150 mg/months	No response	No response Switch to Secukinumab 300 mg/ month			
Subject 5	Start Secukinumab 150 mg/ month + MTX.	Achievement of partial response	**Achievement of complete response** Discontinuation of MTX for achievement of complete response			

CLINICAL SCIENCE

Long-term effectiveness and safety of secukinumab for treatment of refractory mucosal and articular Behçet's phenotype: a multicentre study

Filippo Fagni,[1] Alessandra Bettiol,[2] Rosaria Talarico ,[3] Giuseppe Lopalco ,[4] Elena Silvestri,[1] Maria Letizia Urban,[1] Paul A J Russo,[5] Gerardo Di Scala ,[1] Giacomo Emmi,[1] Domenico Prisco[1]

- 15 CD, cDMARD , en az 1 TNF dirençli mukokutanöz, artrit

	Baseline	Month 3	P value*	Month 6	P value*	Month 12	P value*	Month 18	P value*	Month 24	P value*
Number of observations	15	15		15		13		10		8	
Overall response	–	10 (66.7)		13 (86.7)		10 (76.9)		9 (90.0)		8 (100.0)	
Complete response	–	4 (26.7)		7 (46.7)		7 (53.9)		5 (50.0)		7 (87.5)	
Partial response	–	6 (40.0)		6 (40.0)		3 (23.1)		4 (40.0)		1 (12.5)	
No response	–	5 (33.3)		2 (13.3)		3 (23.1)		1 (10.0)		0	
Control of the mucosal and articular involvements											
Number of oral ulcers in the last 28 days Median (IQR)	2 (2–3)	1 (0–1)	0.006†	0 (0–1)	<0.001†	0 (0–0)	0.002†	0.5 (0–1)	0.005†	0 (0–0)	0.012†
Mean±SD	2.4±1.4	0.9±1.2		0.3±0.6		0.4±0.9		0.5±0.5		0.1±0.4	
DAS28 Median (IQR)	3.9 (2.9–4.2)	2.6 (2.2–3.1)	0.005†	2.5 (2.0–2.9)	<0.001†	2.6 (1.9–3.4)	0.011†	2.2 (2–2.3)	0.005†	2.1 (1.6–2.4)	0.012†
Mean±SD	3.8±0.8	2.9±0.9		2.4±0.6		2.6±0.8		2.2±0.7		2.0±0.6	
Relapse	–	–		1 (6.7)		3 (25.1)		4 (40.0)		0 (0)	

Pharmacology and Treatment

Dermatology

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Mycophenolate Mofetil Is Ineffective in the Treatment of Mucocutaneous Adamantiades-Behçet's Disease

Y.D. Adler[a] U. Mansmann[b] Ch.C. Zouboulis[a]

[a]Department of Dermatology and [b]Institute of Medical Informatics, Biometry and Epidemiology, University Medical Center Benjamin Franklin, The Free University of Berlin, Germany

Mycophenolate sodium in the treatment of mucocutaneous Behcet's diseases

International Journal of Dermatology 2011, **50**, 893–900

10 BH
6 ay sonra mukokütanöz bulgularda iyileşme

Recommendation

2018 update of the EULAR recommendations for the management of Behçet's syndrome

Gulen Hatemi,[1] Robin Christensen,[2] Dongsik Bang,[3] Bahram Bodaghi,[4] Aykut Ferhat Celik,[5] Farida Fortune,[6] Julien Gaudric,[7] Ahmet Gul,[8] Ina Kötter,[9] Pietro Leccese,[10] Alfred Mahr,[11] Robert Moots,[12] Yesim Ozguler,[1] Jutta Richter,[13] David Saadoun,[14,15,16,17] Carlo Salvarani,[18] Francesco Scuderi,[19] Petros P Sfikakis,[20] Aksel Siva,[21] Miles Stanford,[22] Ilknur Tugal-Tutkun,[23] Richard West,[24] Sebahattin Yurdakul,[1] Ignazio Olivieri,[25] Hasan Yazici[1]

- Oral ve genital ülserlerin tedavisinde steroidler gibi topikal önlemler kullanılmalıdır.
- Özellikle baskın lezyon eritema nodozum veya genital ülser olduğunda tekrarlayan mukokutanöz lezyonların önlenmesi için ilk önce kolşisin denenmelidir.
- Papülopüstüler veya akne benzeri lezyonlar, akne vulgariste olduğu gibi topikal veya sistemik önlemlerle tedavi edilir.
- BS'deki bacak ülserleri venöz staz veya obliteratif vaskülitten kaynaklanabilir. Tedavi mutlaka dermatolog ve damar cerrahının yardımıyla planlanmalıdır.
- Azatioprin, talidomid, interferon-alfa, TNF-alfa inhibitörleri veya apremilast gibi ilaçlar seçilmiş vakalarda düşünülmelidir.

	Skin and mucosa
Colchicine	
Apremilast	
Azathioprine	
Cyclosporine-A	
Cyclophosphamide	
Interferon-alpha	
TNF inhibitors	
IL-1 inhibitors	
IL-6 inhibitor	
IL-17 inhibitor	
IL-23 inhibitor	

	Effective based on RCTs		Contraversial / inconclusive data
	Beneficial based on non-randomized data		Reported to cause relapses
	Not effective		Not evaluated

Hatemi G. Rheum Dis Clin N Am 49 (2023) 585–602