



LİKEN PLANUS GÜNCEL TEDAVİ

Prof. Dr. Asena Çiğdem Doğramacı
Mustafa Kemal Üniversitesi
Tıp Fakültesi, Hatay

LİKEN PLANUS

- Deri, saç folikülleri ve müköz membranları etkileyen kaşıntılı, inflamatuvar yaygın bir hastalıktır.



› J Eur Acad Dermatol Venereol. 2020 Jul;34(7):1403-1414. doi: 10.1111/jdv.16464.

European S1 guidelines on the management of lichen planus: a cooperation of the European Dermatology Forum with the European Academy of Dermatology and Ven

D Ioannides^{1, I}
J Ronnevig^{7, T}
M Neumann¹²

Therapeutic strategies for oral lichen planus: State of the art and new insights

Dario Didona^{1*}, Raffaele Dante Caposiena Caro², Antonio Manuel Sequeira Santos¹, Farzan Solimani^{3,4} and Michael Hertl¹

1. basamak

- Topical steroids
- Intralesional steroids
- Systemic corticosteroids
- Acitretin/isotretinoin
- Cyclosporine

2. basamak

- Topical calcineurin inhibitors
- Phototherapy (UVB or PUVA)
- Combination of phototherapy and acitretin
- Sulphasalazine

3. basamak

- Hydroxychloroquine
- Azathioprine
- Mycophenolate mofetil
- Methotrexate
- Apremilast
- Ustekinumab
- Topical calcipotriol
- Antibiotic treatment (trimethoprim-sulphomethoxazole, metronidazole)
- Antifungal therapy (itraconazole, terbinafin, griseofulvin)
- Cyclophosphamide
- Thalidomide
- Adalimumab
- Interferon $\alpha 2b$
- Alitretinoin
- Low molecular weight heparin
- Photodynamic therapy
- Extracorporeal photochemotherapy

Study	Lichen planus	Intervention	Target	Design	Phase	Status
NCT03697460	Cutaneous LP	INCB018424 (Ruxolitinib)	JAK1/2	Single center, exploratory, open-label, single-arm	2	Completed (2021)
NCT03656666	Genital erosive LP	Apremilast	PDE4	Double-blinded, randomized, placebo-controlled	2	Recruiting (2021)
NCT05030415	Lichen planopilaris and LP	Ixekizumab	IL17A	Open-label		Recruiting (2021)
NCT04300296	Lichen planopilaris, oral and cutaneous LP	Secukinumab	IL17A	Multicenter, randomized, double-blind, placebo-controlled	2	Active, not recruiting (2021)
NCT03417141	Lichen planopilaris	Mechlorethamin (Valchlor)	-	Open-label	2	Completed (2021)
NCT04409041	Lichen planopilaris and frontal fibrosing alopecia	Naltrexone	Opiate-receptor	Open-label	2	Completed (2021)
NCT03858634	Pruritus, CIU, LP, Lichen simplex chronicus, plaque psoriasis	Vixarelimab (KPL-716)	Oncostatin M receptor beta	Quadruple -blinded, randomized	2	Completed (2020)
NCT04976673	Oral LP	PDT	-	Double-blinded, randomized	2	Completed (2021)
NCT01282515	Female genital erosive LP	PDT	-	Single (investigator)-blinded, randomized	2/3	Completed (2021)
NCT04991012	Oral LP	PDT	-	Double-blinded, randomized	2	Completed (2021)

Biyolojik tedaviler

- 2017'de sekukinumab ile tedavi edilen psoriasis hastasında oral LP-yan etki candida?
- Anti IL17 tedavisi sırasında 3 vaka daha tanı: likenoid infiltrat

Ghiam N, Ojong O, Vasile G, Romanelli P, Kerdel F. Lichenoid drug eruption after treatment with ixekizumab for plaque psoriasis. *Dermatol Online J.* (2020)

- 5 LP tanılı hasta, anti IL17 tedavisi başarılı

Rezzag-Mahcene C, Cardot-Leccia N, Lacour JP, Montaudié H, Passeron T. Successful treatment of recalcitrant genital lichen planus with secukinumab. *J Eur Acad Dermatol Venereol.* (2021)

Anti IL12/23 (Ustekinumab)

- 1 hastada tedavi başarısız

Webster G. Failure of lichen planopilaris to respond to ustekinumab. Dermatol Online J. (2015)

- 3 LP ve 1 LP pemfigoides hastasında başarılı

Knisley RR, Petropolis AA, Mackey VT. Lichen planus pemphigoides treated with ustekinumab. Cutis. (2017)

Ismail FF, Sinclair R. Clinical healing of erosive oral lichen planus with tildrakizumab implicates the interleukin-23/interleukin-17 pathway in the pathogenesis of lichen planus. Australas J Dermatol. (2020)

NOT: Ne IL12/23 inh ne de IL23 inh ile LP'un tetiklendiği hiçbir vaka bildirilmemiş.

- Anti TNF tedavi ile literatürde çok sayıda likenoid ilaç erupsiyonu bildirilmiştir.
- Tedaviye cevap veren tek vaka Adalimumab ile

Hollo P, Szakonyi J, Kiss D, Jokai H, Horvath A, Karpati S. Successful treatment of lichen planus with adalimumab. Acta Derm Venereol. (2012)

JAK inh

- Tofasitinib (JAK1/3selektif inh) ile iki bağımsız çalışmanın sonucunda 13 hastanın 11'inde düzelme

Pietschke K, Holstein J, Meier K, Schäfer I, Müller-Hermelink E, Gonzalez-Menendez I, et al.. The inflammation in cutaneous lichen planus is dominated by IFN- γ and IL-21-A basis for therapeutic JAK1 inhibition. *Exp Dermatol.* (2021)

Barrat FJ, Crow MK, Ivashkiv LB. Interferon target-gene expression and epigenomic signatures in health and disease. *Nat Immunol.* (2019)

Solimani F, Pollmann R, Schmidt T, Schmidt A, Zheng X, Savai R, et al.. Therapeutic Targeting of Th17/Tc17 Cells Leads to Clinical Improvement of Lichen Planus. *Front Immunol.* (2019)

- Topikal ruxolitinib çalışmaları

Apremilast

- Çok güçlü antiinflamatuvar etkili PDE4 inh.
- 2 × 20 mg/gün apremilast 12 hafta başarılı (2013)
- Genital eroziv LP çalışmaları devam ediyor.

Skullerud KH, Gjersvik P, Pripp AH, Qvigstad E, Helgesen ALO. Apremilast for genital erosive lichen planus in women (the AP-GELP Study): study protocol for a randomised placebo-controlled clinical trial. *Trials*. (2021)

Diğerleri

- Opioid reseptör antagonisti Naltrexone (LPP)
- Topikal mechloroethamine (kemoterapi)
- Fotodinamik tedavi (PDT)
- Dar bant UVB ve PUVA

Weber B, Marquart E, Radakovic S, Tanew A. Effectiveness of narrowband UVB phototherapy and psoralen plus UVA photochemotherapy in the treatment of generalized lichen planus: results from a large retrospective analysis and an update of the literature. *Photodermatol Photoimmunol Photomed.* (2021).

- Ekstrakorporeal fotokemoterapi (ECP)

ORAL LP

- Oldukça yaygın görülen genellikle oral mukozanın çok katlı yassı epitel tabakasını etkileyen kronik inflamatuvar bir hastalıktır.
- Ortalama olarak popülasyonun %1-2'sini etkilemekle birlikte sıklıkla 3-6 dekat aralığında ve kadınlarda, erkeklere oranla 2 katı daha fazla görülmektedir.
- OLP'nin etyolojisinde immün sistemin rol oynadığı düşünülmektedir.



İlk basamak tedavi

- Topikal steroidler (Klobetasol propionate %0.05, triamcinolone, betamethasone)
- Sistemik kortikosteroidler
- Sistemik retinoidler (asitretin)
- Topikal retinoidler (isotretinoin %0,05-0,1)
- Oral siklosporine (3-10mg/kg/gün)

2. Basamak Tedavi

- Topikal kalsinörin inh (pimekrolimus, takrolimus)
- Sulfasalazin (2.5mg/gün 6 hafta)
- Azatiopurin
- Hidroksiklorokin
- Methotreksate
- Mikofenolat mofetil
- TNF α inh.

Diğer tedaviler

Cyclophosphamide (100 mg/day),⁷³

Thalidomide¹⁰⁶ (initial dose of 50 to 100 mg/day and then progressively decreased to the minimal effective dose),

Antibiotic treatment for 1–3 month (metronidazole – 250 mg every eight hours daily-⁶⁶, trimethoprim–sulphomethoxazole, tetracycline 500 mg twice daily, doxycycline 100 mg twice daily),⁶⁹

Itraconazole⁶⁷, griseofulvin,¹⁰⁷

Dapsone (initial dose of 50 mg/day is given for the first 15 days, and then, the dose is increased to 100 mg/day),¹⁰⁸

Low molecular weight heparin (enoxaparin 3 mg/week),¹⁰⁹

Interferon has been used as a treatment modality in cases of LP associated with hepatitis C¹¹⁰

Levamisole (50 mg thrice daily or 150 mg once daily, for three consecutive days per week for at least 3 months),¹¹¹

Lycopene (8 mg/day for 8 weeks),¹¹²

Purslane (235 mg/day),¹¹³

Curcuminoids (6000 mg/day 3 divided doses),¹¹⁴

Aloe vera¹¹⁵

Topical tocopherol¹¹⁶

Colchicine¹¹⁷

0.5 mL of intralesional BCG (bacillus Calmette-Guerin) injection¹¹⁸ was used every other day for two weeks and proved to be as effective as 10 mg triamcinolone acetonide injections every week for 2 weeks.

Extracorporeal photochemotherapy¹¹⁹

Psoralen plus UVA (PUVA), UVA₁, broadband or narrowband UVB¹²⁰

Er: YAG laser (2940 nm),¹²¹ diode laser (630 nm),¹²² carbon dioxide laser

56 eroziv oral LP

- 31'ine lezyon içi 10mg/ml triamsinolon asetonid
%88
- 25'ine lezyon içi 0,5 ml. BCG
%87.1

Xiong C, ve ark. J Oral Pathol Med 2009.

13 oral eroziv LP hastası

- yanak mukozalarının bir tarafına i-PRF, diğer tarafına intralezyonel kortikosteroid enj.
- Enjeksiyonlar 15 gün araya 4 seans
- Bu pilot çalışma, i-PRF enjeksiyonunun EOLP lezyonların tedavisinde altın standart kabul edilen kortikosteroid enjeksiyonuna benzer derecede etkili olabileceğini göstermiş

- 3 eroziv LP ve 1 hipertrofik LP → Tofacitinib (JAK1-3 inh) etkili
- 10 liken planopilariste yine etkili bulunmuş.
- Upadasitinib (JAK 1 inh) → 12. haftada nazofaringeal ağrı ve disfajide belirgin azalma, 24 haftada lezyonlarda kaybolma

Correspondence Clinical Letter

Clinical Letter

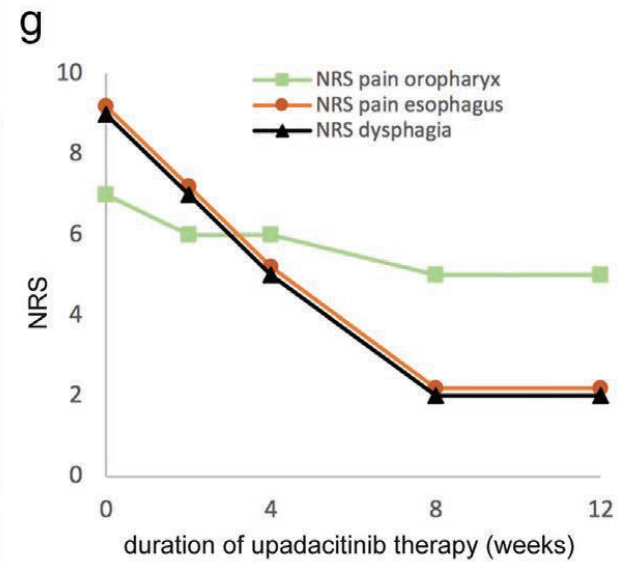
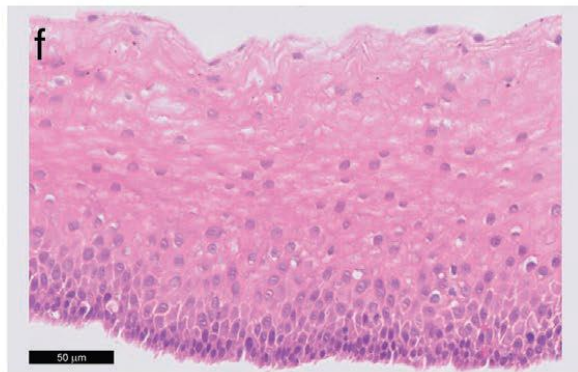
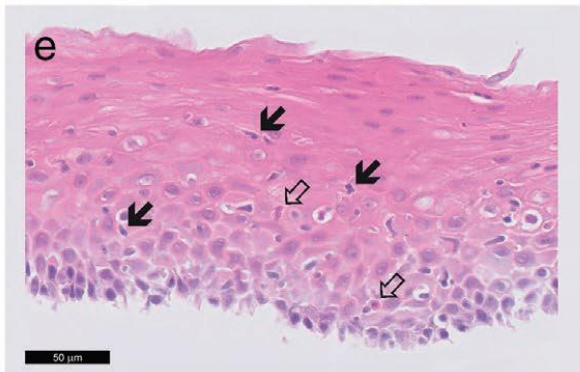
Alleviation of erosive oral and esophageal lichen planus by the JAK1 inhibitor upadacitinib

DOI: 10.1111/ddg.14612

Before upadacitinib therapy, the patient rated the pain in her oropharynx as 7/10 on a numerical rating scale (NRS), and esophageal pain as well as dysphagia were rated as 9/10 on the NRS. After only four weeks of therapy with upadacitinib, disease activity had decreased considerably. The oral mucosa was no longer erosive and no further deterioration occurred (Figure 1a, b). After twelve weeks, the oropharyngeal NRS had reduced to 5/10, and the NRS for both esoph-

- 1 oral LP hastası → Barisitinib ile etkili tedavi

Moussa A, Colla T, Morrison B, Sinclair R. Effective treatment of oral lichen planus with the JAK inhibitor baricitinib. Australas J Dermatol. (2022)



Oral LP tedavisinde biyolojikler

Drug	Number of patients	Treatment period	Observation period	Comment
Adalimumab (29)	1	50 weeks	50 weeks	Clinical improvement
Adalimumab (30)	1	12 weeks	12 weeks	Complete healing
Alefacept (34)	2	12 weeks	32 weeks	Clinical improvement
Alefacept (33)	2	12 weeks	12 weeks	Clinical improvement
Etanercept (28)	1	10 weeks	17 weeks	Clinical improvement and pain relief after etanercept; disease recurrence after agent discontinuation
Guselkumab (15)	1	30 weeks	30 weeks	Complete healing
Infliximab (27)	1	6 months	6 months	Clinical improvement
Rituximab (37)	1	4 weeks	10 months	Clinical improvement; relapse after 10 months
Rituximab (35)	2	14 months	14 months	Remission lasted until 8 months
Rituximab (38)	5	4 months	9 months	Clinical improvement
Secukinumab (15)	3	12–48 weeks	12–48 weeks	Complete healing
Tildrakizumab (16)	1	28 weeks	28 weeks	Complete healing
Ustekinumab (15)	1	48 weeks	48 weeks	Complete healing

Tırnakta LP

- Ungual LP genellikle tedaviye çok dirençlidir. Bu subtipin prognozu kötüdür, rekürrens hızı yüksektir.
- Tedavi pterjium ya da total tırnak kaybı gibi irreversible değişiklikler olmadan hızlıca başlanmalıdır.
- Yine de ancak %50 hastada kür elde edilebilir.

ilk basamak tedavi

- Triamsinolon enj 0.5mg/kg/ay İM
- İL olarak 0.1-0.5 mg/2 ayda bir
- Oral prednison 0.5mg/kg 3 hafta

Diğer tedaviler

Asitretin

Takrolimus günde 2 kez/6 ay

Alitretinoin (30mg/gün 3-6 ay)

Klorokin fosfat (500mg 10-30 hafta)

Fluorasil %5 topikal

Biotin 2.5 mg (çocuklarda) 7.5-10 mg (erişkin) 6 ay

Etanercept

Liken planopilaris

1. basamak tedavi

Topical steroids (superpotent, potent, mild)

Intralesional injection of corticosteroids (e.g. triamcinolone 5-20 mg/mL every 2–4 weeks)

Systemic steroids (30–80 mg/day of prednisone)

Cyclosporine in systemic administration (3–10 mg/kg/day)

Hydroxychloroquine sulphate (200–400 mg/day or 6.5 mg/kg per day for 6 to 12 months)^{128, 133, 135}

Methotrexate (15 mg/weekly for 6 months)¹³⁶

Topical calcineurin inhibitors, primarily tacrolimus¹³⁴

2. basamak tedavi

- Sistemik retinoidler (özellikle perifoliküler hiperkeratoz varsa)
- Tetrasiklin/doksisiklin (100mg/gün 1 ay)
- Mycofenolat mofetil (1 gr 4 hafta sonra 2 gr en az 20 hafta)
- Adalimumab
- Pioglitazone
- Minoxidil %5
- Thalidomid (100-300 mg/gün)
- Rituksimab
- 308 nm excimer lazer

Sonuç;

- LP tedavisi için umut verici gelişmeler olmakla birlikte özellikli subtiplerin tedaviye dirençli olduğu unutulmamalıdır.
- Erken tedavi ile kalıcı destrüksiyonlar engellenebilir.



TEŞEKKÜR EDERİM