EDF S1 Guidelines on the management of Lichen Planus

Developed by the Guideline Subcommittee “Lichen planus” of the
European Dermatology Forum

Subcommittee Members:
Prof. Dr. Dimitrios Ioannides, Thessaloniki (Greece)
Prof. Dr. Efstratios Vakirlis, Thessaloniki (Greece)
Prof. Dr. Layos Kemeny, Szeged (Hungary)
Prof. Dr. Branka Marinovic, Zagreb (Croatia)
Dr. Cesare Massone, Graz (Austria)
Dr. Ruth Murphy, Nottingham (United Kingdom)
Prof. Dr. Alexander Nast, Berlin (Germany)
Dr. Jørgen Ronnevig, Oslo (Norway)
Prof. Dr. Thomas Ruzicka, Munich (Germany)
Dr. Sue M. Cooper, Oxford (United Kingdom)
Prof. Dr. Ralph M. Trüeb, Wallisellen (Switzerland)
Prof. Dr. Ramon M. Pujol Vallverdú, Barclelona (Spain)
Prof. Dr. Ronald Wolf, Marburg (Germany)
Prof. Dr. Fenella Wojnarowska, Oxford (United Kingdom)
Prof. Dr. Martino Neumann, Rotterdam (Netherlands)

Members of EDF Guideline Committee:
Prof. Dr. Werner Aberer, Graz (Austria)
Prof. Dr. Martine Bagot, Paris (France)
Prof. Dr. Nicole Basset-Seguin, Paris (France)
Prof. Dr. Ulrike Blume-Peytavi, Berlin (Germany)
Prof. Dr. Lasse Braathen, Bern (Switzerland)
Prof. Dr. Sergio Chimenti, Rome (Italy)
Prof. Dr. Alexander Enk, Heidelberg (Germany)
Prof. Dr. Claudio Feliciani, Parma (Italy)
Prof. Dr. Claus Garbe, Tübingen (Germany)
Prof. Dr. Harald Gollnick, Magdeburg (Germany)
Prof. Dr. Gerd Gross, Rostock (Germany)
Prof. Dr. Michael Hertl, Marburg (Germany)
Prof. Dr. Dimitrios Ioannides, Thessaloniki (Greece)
Prof. Dr. Gregor Jemec, Roskilde (Denmark)
Prof. Dr. Lajos Kemény, Szeged (Hungary)
PD Dr. Gudula Kirtschig, Tübingen (Germany)
Prof. Dr. Robert Knobler, Vienna (Austria)
Prof. Dr. Annegret Kuhn, Muenster (Germany)
Prof. Dr. Marcus Maurer, Berlin (Germany)
Prof. Dr. Dieter Metze, Muenster (Germany)
Prof. Dr. Kai Munte, Rotterdam (Netherlands)
Prof. Dr. Gillian Murphy, Dublin (Ireland)
Prof. Dr. Alexander Nast, Berlin (Germany)
Prof. Dr. Martino Neumann, Rotterdam (Netherlands)
Prof. Dr. Tony Ormerod, Aberdeen (United Kingdom)
Prof. Dr. Mauro Picardo, Rome (Italy)
Prof. Dr. Annamari Ranki, Helsinki (Finland)
Prof. Dr. Johannes Ring, Munich (Germany)
Prof. Dr. Berthold Rzany, Berlin (Germany)
Prof. Dr. Rudolf Stadler, Minden (Germany)
Prof. Dr. Sonja Ständer, Münster (Germany)
Prof. Dr. Wolfram Sterry, Berlin (Germany)
Prof. Dr. Eggert Stockfleth, Bochum (Germany)
Prof. Dr. Alain Taieb, Bordeaux (France)
Prof. Dr. George-Sorin Tiplica, Bucharest (Romania)
Prof. Dr. Elke Weisshaar, Heidelberg (Germany)
Prof. Dr. Sean Whittaker, London (United Kingdom)
Prof. Dr. Fenella Wojnarowska, Oxford (United Kingdom)
Prof. Dr. Andreas Wollenberg, Munich (Germany)
Prof. Dr. Christos Zouboulis, Dessau (Germany)
Prof. Dr. Dr. Torsten Zuberbier, Berlin (Germany)

Chairman of EDF Guideline Committee:
Prof. Dr. Alexander Nast, Berlin (Germany)

Expiry date: 03/2022

EDF Guidelines Office to Professor Dr. Nast:
Martin Dittmann, Klinik für Dermatologie, Venerologie und Allergologie, Campus Charité Mitte,
Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany
phone: +49 30 450 618 313, fax: +49 30 450 518 977, e-mail: martin.dittmann@charite.de

EDF S1 Guidelines on the management of Lichen Planus

Dimitrios Ioannides[1], Efstratios Vakirlis[1], Lajos Kemeny[2], Branka Marinovic[3], Cesare Massone[4], Ruth Murphy[5], Alexander Nast[6], Jørgen Ronnevig[7], Thomas Ruzicka[8], Sue M. Cooper[9], Ralph M. Trüeb[10], , Ramon M. Pujol Vallverdú[11], Ronald Wolf[8], Fenella Wojnarowska[12], Martino Neumann[13]

1. Department of Dermatology and Venereology, Aristotle University of Thessaloniki Medical School, Greece

2. Department of Dermatology and Allergology, University of Szeged, Hungary

3. Department of Dermatology and Venereology, University Hospital Center and School of Medicine Zagreb, Croatia

4. Department of Dermatology, Medical University of Graz, Austria

5. Department of Dermatology, Nottingham University Hospital, Nottingham, UK

6. Charité - Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Department of Dermatology, Venereology and Allergy, Division of Evidence-Based Medicine, Department of Dermatology, Charité, Berlin.

7. Oslo University Hospital, Oslo, Norway

8. Department of Dermatology and Allergology**,** LMU, Munich, Germany

9. Department of Dermatology, Oxford University Hospitals, NHS Trust and University of Oxford, Oxford, UK.

10. Center for Dermatology and Hair Diseases, Wallisellen, Switzerland

11. Department of Dermatology, Hospital del Mar, Barcelona, Spain

12. Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK.

13. Department of Dermatology, Erasmus MC, Rotterdam, The Netherlands

Corresponding author:

Professor Dimitrios Ioannides
Head, 1st Department of Dermatology and Venereology,
Aristotle University Medical School,
Hospital of Skin and Venereal Diseases - Hippokration General Hospital
Thesssaloniki, Greece
Tel.: (+30) 2310-992262
Fax: (+30)2310-992221
Email: dem@auth.gr
Mobile: +306948109109

Table of Contents

INTRODUCTION

Lichen planus (LP) is a common mucocutaneous disease affecting stratified squamous epithelia. The etiology of the condition is complex and multifactorial, with histopathological features more typical in cutaneous than mucosal lesions, where ulceration is more apparent. LP most commonly affects middle-aged adults, in particular peri-menopausal women and is rare in children. The lesions usually involve the skin (cutaneous lichen planus), the oral cavity (oral lichen planus), the genitalia (penile or vulvar lichen planus), the scalp (lichen planopilaris), nails (lichen unguis), or extra-cutaneously (e.g. the esophagus). The diagnosis and management of lichen planus will be reviewed here.

Despite the high prevalence of the disease and the variety of therapeutic options available, no national or international evidence-based guidelines for treatment exist. That is why the European Dermatology Forum (EDF) initiated a project to develop guidelines for the treatment of lichen planus. Based on expert opinion and literature search, therapeutic recommendations were developed through round mailing (Delphi method). This process was subject to an approval of the guidelines by all the members of the sub-Committee.

The purpose of the guideline is to provide all health care professionals with a tool for choosing an efficacious and safe therapy for various subgroups of patients, presenting with different subtypes of lichen planus. Health care professionals include dermatologists, dentists, gynecologists, urologists, general practitioner in clinics, as well as in private practice and other specialists who are involved in the treatment of patients with lichen planus.

METHODS

These guidelines were conducted as S1 – Guidelines for the treatment of lichen planus. Evidence for this guideline was provided by review of the literature of the databases Medline/Pubmed, EMBASE and Cochrane Library from 1/1/1986 to October 2018, using the term lichen planus, diagnosis, treatment, therapy and prognosis.

The evaluations of these guidelines are restricted on the efficacy of the particular therapeutic options and based on opinions and personal experiences of the members of the

guideline group and the evaluation of the level of evidence of the studies. All recommendations were agreed on in a round mailing consensus. A list of possible treatments for each LP subtype was prepared and sent to all authors. All nominated experts were entitled to report their choice of preferable treatments for each LP subtype in a numerical order. Therefore, the highest possible consensus level of treatment preference was reached.

The resulting therapeutic recommendations aim to optimize the therapeutic process and to support the healthcare practitioner in the individual decision on a suitable therapy.

DEFINITION

Lichen planus is an inflammatory skin disease affecting the skin, mucous membranes, hair and nails. The term lichen planus is derived from the Greek word “leichen”, which means *to lick or what eats around itself*, describing the characteristic way this skin disease appears and evolves and the Latin word “planus”, which means *“flat”,* depicting the specific appearance of this disorder. The dermatosis was first described by Erasmus Wilson in 1869.[1]

Lichen planus is a distinctive entity that affects various areas of the body, either concomitantly or sequentially. It is a chronic inflammatory disease, with the exception of most cutaneous forms, that often resolves spontaneously within one to two years. Skin hypertrophic and mucosal lichen planus are considered a potential premalignant condition, as the incidence of squamous cell carcinoma in these LP variants is approximately 1%.[2,3,4,5]

Three systematic reviews were prepared on the treatment of oral and erosive mucosal LP respectively[6,7,8] , four on the treatment of cutaneous lichen planus[9,10,11,12], and one on the therapeutic management of lichen planopilaris.[13] Data from randomized, controlled trials are limited, and management choices are based mainly on clinical experience.[3,10]

EPIDEMIOLOGY

Estimations on the incidence of lichen planus are between 0.14 and 1.27% of the general population.[2] At least two-thirds of the cases occur between the ages of 30 and 60 years. The disease is uncommon in children; however it can occur at any age. No sexual or racial prevalence is evident in the cutaneous form, whereas 60 to 75% of patients with oral lichen planus are females.[3] The prevalence of oral lichen planus is approximately 1,5%.[4] Familial cases are rare, but have been described.[14]

PATHOPHYSIOLOGY-ETIOPATHOGENESIS

The pathogenesis of LP remains unclear, but it is likely to be of a multi-factorial nature. It is generally considered an immunologically mediated disorder. It affects surfaces covered by stratified squamous epithelium.

There is evidence that cell-mediated immune response plays a major role in the development of the disease. T cells, both CD4+ and CD8+, accumulate in the dermis, while CD8+ T cells infiltrate the epidermis in LP lesions. The majority of lymphocytes in the LP infiltrate consists of CD8+ and CD45RO+ cells and expresses the α-β T cell receptor (TCR), and to a lesser extent the γ-δ receptor.[15] These cells are responsible for the most characteristic change observed in the lichenoid reaction, apoptosis.[2]
Genetic and environmental factors, such as stress, infections (e.g. HPV[16], HSV[17]), changes in the mucosal microbiome (e.g. Candida sp, various other bacteria[18]) and dental amalgam play an important role for disease manifestation. Genetic susceptibility has been documented. Different haplotypes, such as HLA –A3, -A5, -A28, -B8, -B16, -Bw35, -B7, -B18, -Aw19, -Cw8 are associated with different variants of LP.[14]

Disease associations

A significantly high prevalence of thyroid disease among OLP patients has been observed, [19] whereas contradictory results were found when analyzing the relationship between lichen planus and diabetes mellitus.[20] Other diseases of altered immunity, particularly alopecia areata, ulcerative colitis, vitiligo, morphea, lichen sclerosus and myasthenia gravis, occur more frequently in patients with LP. Patients with lichen planus present a higher risk for dyslipedemia, which could be explained by the cytokines involved in the pathogenesis of the

disease, such as TNF-a, IL-6, IL-10, and IL-4. Therefore lipid level screening in LP patients is recommended to detect individuals at risk for the development of cardiovascular diseases.[21]

Certain disorders and infections, such as hepatitis C, [22,23] hepatitis B (lichen planus pemphigoides),[24] hepatitis B[25] vaccination and primary billiary cirrhosis are associated with LP. In contrast, specifically for hepatitis C, there are studies suggesting that there is no association between the two disorders or that such an association is geographically dependent.[26,27,28] Therefore, hepatitis C tests are recommended in LP patients from regions (Africa, Middle East and Asia) with high prevalence of the infection.

There are also specific medications, which are considered responsible for drug-induced lichen planus (a relevant list is included under the "LP and its variants" part of the Guidelines).[28,29,30]

CLINICAL PICTURE

Lichen planus is a unique entity representing skin and mucosal lesions of typical color, morphology and distribution. Classical cutaneous lichen planus is characterized by pruritic, flat-topped, polygonal violaceous papules localized to the wrists, forearms, distal lower extremities and the pre-sacral area. The lesions on non-keratinised epithelium, such as the buccal mucosa, tongue, esophagus and genitalia are often non-pruritic and may present with burning or being entirely non symptomatic. Mucosal lesions become often erosive. LP affecting the hair follicles and the nail bed will often lead to permanent scarring resulting in islands of alopecia and pterygium formation with eventual loss of the nail plate.[2,14]

LP onset is usually acute with initial lesions almost always appearing on the extremities. A generalized eruption, in approximately one-third of the cases, may be developed after one week or more with maximal spreading within 2-16 weeks.

Papules are grouped and tend to coalesce and sometimes form a central umbilication. They are usually distributed symmetrically and bilaterally over the extremities and often covered by lacy, reticular, white lines known as Wickham striae. This fine, whitish punctae are

considered highly characteristic and observed more easily after applying oil, xylene or water when visualizing the lesions with a magnifying lens or a dermatoscope. The lesions may also appear in a linear configuration, following the lines of trauma (isomorphic response, Koebner phenomenon). The development of the disease usually lasts several weeks. The lesions spread within 1-4 months from onset.

Pruritus of varying severity is the characteristic symptom reported by the patients, and depends on the type of lesions and extent of involvement. Some of the affected patients may be completely asymptomatic (approximately 20%) and oral lesions may have a burning sensation or may even be painful.

Classical cutaneous LP is self-limited and usually resolves within 6 (>50%) to 18 months (85%). Chronic disease is more typical in hypertrophic cutaneous lesions, orogenital lichen planus, and with nail or scalp involvement. Hyperpigmentation as a result of inflammation is often present especially in individuals with darker skin and can become very impacting.[2,14] Lichen planopilaris in the muzzle region is particularly problematical in this respect.

DIAGNOSIS (HISTOLOGICAL AND IMMUNOFLUORESCENCE FEATURES)

The diagnosis of LP relies on the typical morphology of lesions at the affected site with histopathological correlation.

Histopathology: Mucocutaneous biopsies can confirm the diagnosis, especially when taken from the edge of a classical plaque. At this site, the characteristic histology is a dense, band-like lymphocytic infiltrate, which is seen in the upper dermis underlying a variably acanthotic epidermis with hyperkeratosis, wedge-shaped hypergranulosis related to the acrosyringia and vacuolisation of the basal layer of the epidermis with scattered apoptotic cells (Civatte bodies).

Small clefts may be present at the dermo-epidermal junction, but a clear subepidermal blister is typical only of bullous variant. The epidermis is atrophic, hyperplastic or ulcerated in atrophic, hypertrophic or erosive/ulcerative clinical variants, respectively. A biopsy from a

central part on an ulcerated area will often reveal an inflammatory response with plasma cells and lymphocytes and an absence of any typical features. Melanin incontinence with melanophages is usually variable but prominent only in hyperpigmented clinical variants. Eosinophils may be seen in drug induced lesions. In follicular variants, the lichenoid reaction involves the basal layer of the follicular epithelium; variable degrees of perifollicular fibrosis may be seen.[30]

Immunofluorescence features: Direct immunofluorescence (DIF) testing reveals globular deposits of several immunoglobulins, especially IgM and complement or fibrinogen mixed with apoptotic keratinocytes (Civatte bodies). There is a report of 6 cases with linear appearance.[31] DIF with a sensitivity of 75% [32] is particularly helpful in differentiating erosive LP from immunobullous diseases, such pemphigus vulgaris.

Dermatoscopic findings: they consist of white crossing lines (Wickham sign), dull red background, and peripheral arrangement of vessels.[33,34]

Other assays: it has been proposed that future diagnostic adjuncts could include cytokine profiling of involved tissue. However, as other available tests are reasonably accurate for the diagnosis of LP, this is unlikely to become a widely used assay for LP.[35]

Patch tests in patients with LP usually reveal positive results, which are not associated with specific variants of cutaneous LP or the prognosis of the disease. Patch testing is better to be included in the work up of oral LP, where oral lesions show proximity to dental restorations.[36] The material of these restorations can aggravate or induce the lichenoid reaction. [36]

No imaging studies are necessary for the diagnosis of lichen planus.

Differential diagnosis

There are many disorders to be considered in the differential diagnosis of lichen planus:

- Lichen nitidus, Lichen sclerosus, Lichen spinulosus, Graft versus host disease Lichen striatus, Linear epidermal nevus, Nevus unius lateralis
- Eczema, Lichen simplex chronicus, Prurigo nodularis

- Pityriasis rosea, Guttate Psoriasis, Psoriasis vulgaris, Ekzematid-like Purpura
- Drug eruption, Syphilis, Tinea corporis, Papular acrodermatitis of childhood
- Granuloma annulare, Lichen amyloidosus, Pityriasis lichenoides, Kaposi sarcoma

Table 1. Differential diagnosis of site-specific LP	
Nail	Psoriasis, onychomycosis, alopecia areata, atopic dermatitis
Genital	Lichen sclerosus, mucous membrane pemphigoid, vulval intraepithelial neoplasia, graft vs host disease, psoriasis, seborrheic dermatitis, intertrigo,
Palms and soles	Secondary syphilis, psoriasis vulgaris, warts, calluses, porokeratosis, hyperkeratotic eczema, pityriasis rubra pilaris, tinea, drug reaction, gloves-and-socks-disease
Lichen planopilaris	Cicatrial alopecia, lupus erythematosus, inflammatory folliculitis, alopecia areata, mucous membrane pemphigoid, frontal fibrosing alopecia
Mucosal	Paraneoplastic pemphigus, candidiasis, lupus erythematosus, secondary syphilis, leukokeratosis, traumatic patches, cicatricial pemphigoid

CLINICAL VARIANTS OF LICHEN PLANUS

Several variations have been described, according to 1) the distribution and configuration of lesions, 2) the morphology of an individual lesion, and/or 3) the site of involvement. The various clinical forms were divided into three general categories, namely cutaneous, appendageal and mucosal lichen planus. The specific clinical and histological manifestations are briefly described below (table 2).

Cutaneous LP

1. Localized cutaneous lesions of LP: a) Classical common sites of involvement are wrists, lower legs and lower back. b) Induced LP (Koebner phenomenon), e.g. LP overlying varicose veins. Skin lesions may sometimes form a linear zosteriform pattern (otherwise called linear LP).

2. Generalized cutaneous LP: Widespread eruption, the lesions of which tend to pursue a chronic course. Two thirds of patients with generalized LP have oral mucosal involvement.

3. Palmoplantar LP with localized erythematous scaly plaques: a rare acral localized variant. Highly pruritic, erythematous, scaly plaques with or without hyperkeratosis, localized on the internal plantar arch. Differential diagnosis includes psoriasis vulgaris, warts, calluses, porokeratosis, hyperkeratotic eczema, pityriasis rubra pilaris, tinea, secondary syphilis or lymphoma.

4. Hypertrophic LP localized on the shins and interphalangeal joints (lichen planus verrucosus, calcitriant lichen planus): The most pruritic variant of LP, which is usually found on the extensor surfaces of the lower extremities. Lesions are purplish or reddish-brown in color and hyperkeratotic. Hypertrophic lesions are often persistent and have the potential for malignant transformation (Squamous Cell Carcinoma, SCC). Scarring, hyperpigmentation or hypopigmentation can occur when the lesions eventually clear. Frequently, a chronic venous insufficiency is present.

5. Atrophic LP with few well demarcated atrophic plaques on the trunk and lower extremities: This is a rare variant of LP characterized by a few white-bluish papules or plaques with central superficial atrophy, which are often the resolution of annular or hypertrophic lesions. The lesions usually resemble lichen sclerosus.

6. Vesiculobullous LP with the presence of typical skin lesions. Vesicles and/or bullae arise within some of LP lesions on the extremities. These lesions appear suddenly on the lower limbs or in the mouth on preexisting LP lesions and are usually associated with mild symptoms. The duration of this rare variant is the same with the classic LP.

Histopathology as well as direct and indirect immunofluorescence should be used to differentiate lichen planus pemphigoides from bullous lichen planus.

7. Erosive and ulcerative LP: chronic, painful bullae and ulcerations of the feet, buccal mucosa, alveolar epithelium, sulci, pharynx, laryngeal and esophageal area, which leads to dysphagia and stenosis. These lesions evolve from preexisting LP lesions. This rare variant is usually associated with typical lesions of the nails, mucosal surfaces and skin, which often aids in establishing the diagnosis. Important complications may be observed in this variant: permanent loss of toenails, cicatricial alopecia and potential malignant transformation (SCC).

8. Annular LP: papules that are purely annular are rare. Annular lesions with an atrophic center can be found on the buccal mucosa and male genitalia.

9. LP pigmentosus (ashy dermatosis or erythema dyschromicum perstans) or Actinic LP (LP subtropicus, LP tropicus, summertime actinic lichenoid eruption, LP actinicus, LP atrophicus annularis and lichenoid melanodermatosis). The authors believe that these variants belong to the same entity, representing an overlap in the phenotypic spectrum of lichenoid inflammation in darkly pigmented skin. Patients with darker skin are primarily affected, whereas ethnic and genetic factors may influence the expression of the disease.

   They are common in Latin America, Middle East, Africa and India during spring and summer due to sunlight effect. This mildly pruritic eruption usually affects the sun-exposed areas and spares the covered areas, the nails, the scalp and the mucous membranes. Papules are hyperpigmented with a violaceous-brown color, minimal scaling and well-defined borders. The lesions are characterized by nummular patches, sometimes with a hypopigmented zone surrounding the hyperpigmented center.

10. Lichen planus pemphigoides: A rare and controversial variant. A combination of both

lichen planus and bullous pemphigoid. Blisters subsequently develop on lichen planus lesions. Clinically, histopathologically and immunopathologically it has features of lichen planus and bullous pemphigoid, but with a better prognosis than pemphigoid.

Appendageal LP

1. Lichen planopilaris (LPP) with multifocal hair loss on the scalp (cicatricial alopecia) along with non-cicatricial hair loss on the axilla and pubic area. Typically presents as smooth white patches of the scalp. No hair follicle openings can be seen in the areas of hair loss. At the edges of these patches there may be scale and redness around each hair follicle. Hairs can be easily pulled out. It is multifocal and small patches may merge to form larger irregular areas. Symptoms are often absent but they may include itch, pain, tenderness and burning.

Subtypes:

Frontal Fibrosing Alopecia (FFA): It was first described by Kossard in 1994.[37] Usually affects post-menopausal women over the age of 50 (there are also case reports of FFA in men and in premenopausal women) and is slowly progressive. It is characterized by scarring hair loss of the frontotemporal hairline and may affect the supra-auricular and occipitonuchal hairline, with or without loss of eyebrows, lashes and body hair. Moreover, cicatricial patterned hair loss with a relationship to androgenetic alopecia and a lichenoid inflammatory reaction pattern has been described as Fibrosing Alopecia in a Pattern Distribution (FAPD).

The exact cause of fibrosing alopecia is unknown. Disturbed immune response and hormonal factors thought to be responsible for the disease.

There are also case reports and case series of frontal fibrosing alopecia with the histopathologic features of lichen planopilaris associated or overlapping or even confirm cutaneous lupus erythematosus.

Lassueur-Graham Little syndrome: It rather may occur alone than in association with other forms. Keratotic follicular papules and plaques result in scarring alopecia. The triad of follicular LP of skin or scalp, multifocal cicatricial alopecia of the scalp, and non-

scarring alopecia of the axillary and pubic areas is known as Graham Little-Pidcardi-Lassueur syndrome.

2. LP lesions of the nails (onychoshcysia or/and onychorrhexis or even anonychia). Thinning, longitudinal ridging and distal splitting are the most common findings. Pterygium formation, onycholysis and subungual hyperkeratosis may be less frequently observed.

Mucosal LP

The mucosal lesion of LP can be accompanied by skin lesions. It is believed that mucosal lichen planus is more frequently associated with lesions in other mucosal sites than skin lesions.[38] Non erosive lesions are usually painless, although patients may exhibit a slight roughness on the affected sites. Transformation of mucosal lesions of LP, especially the erosive ones, to squamous cell carcinoma occurs in 1.2 to 5.32% of patients.
The clinical variants of oral lichen planus are well described in an article of the British Society of Oral Medicine.[39] The criteria for diagnosis of genital mucosal LP were recently clearly established.[40]

1. In the oral cavity LP may be plaque-like or erosive. Oral reticulated lesions are common on the gingival, buccal mucosa and the tongue. This is the most common manifestation, presenting as a lacy network of white striations. Erosive lesions may also present with desquamative gingivitis or ulceration particularly along the lateral border of the tongue.

2. Atrophic LP lesions of the oral mucosa. Atrophy can occur within the white patches.

3. Bullous LP of the mucosa. A rare manifestation presenting with small vesicles within the white patches. Genital lesions of LP have been described by the British Society for Sexual Health and HIV and divided in three subtypes.[41]

4. Papular genital LP. Annular lesions or patches of leukoplakia or erythroplakia may be present. Genital LP is frequently missed or misdiagnosed.[42] Patients with lichen planus should always be questioned about genital symptoms.

5. Hypertrophic genital LP. It is a rare variant affecting the perineum and perianal area. Thickened warty plaques can be found and may become ulcerated, infected and painful.

6. Chronic erosive LP lesions in genitalia (vulva and/or vagina or glans penis). The most common subtype in genital clinics. A particular pattern of this form is suggested to be the "vulvovaginogingival or penogingival syndrome", in which an association of erosive genital LP and gingivitis has been observed.

7. Lichen planus of the esophagus. It is considered a rare manifestation of the mucocutaneous disease, which may result in chronic pain, strictures or stenosis. Some authors suggest that screening endoscopy to rule out esophageal involvement may be warranted in all patients with mucocutaneous LP who complain of dysphagia or odynophagia.

Other forms of LP

1. Inverse LP: Lesions of LP confined to intertriginous regions; scales may be absent.

2. Guttate LP: Small lesions are widely scattered, and remain discrete. Differential diagnosis is guttate psoriasis.

3. Perforating LP**:** Lesions of LP from which hyaline bodies are extruded through the epidermis.

4. Invisible LP: Pruritic skin without obvious clinical findings; Wood lamp examination and biopsy may reveal lesions of LP.

5. Overlap syndromes: LP erythematosus: lesions like DLE and LP on the head, neck, upper trunk and extremities. It may progress to SLE. Difficult to treat variant with weak positive antinuclear antibodies.

6. Lichenoid reaction of Graft-Versus-Host-Disease: Clinically and histologically identical lesions like LP.

7. Lichenoid keratosis (Lichen planus like keratosis): Red to brown maculopapules, sometimes scaling on the extremities and pre-sternal areas of middle aged and elderly women.

8. Drug-induced lichen planus: Lesions of lichenoid drug eruption may be identical or similar to those of LP. The patient should be questioned about the use of medications (table 3) known to induce a lichenoid drug eruption, such as[29,43]:

- Antihypertensives – ACE inhibitors, beta-blockers, nifedipine, methyldopa[44]
- Diuretics [45] – hydrochlorothiazide, furosemide, spironolactone
- Non-steroidal anti-inflammatory drugs (NSAIDs)[44]
- Phenothiazine derivatives [46]
- Anti-convulsants – carbamazapine[47], phenytoin
- Drugs to treat tuberculosis[48]
- Antifungal drug – ketoconazole
- Chemotherapeutic agents – hydroxyurea, 5-fluorouracil, imatinib[49]
- Antimalarial agents such as hydroxychloroquine
- Sulfa drugs, including sulfonylurea hypoglycaemic agents, dapsone, mesalazine, sulfasalazine
- Metals – gold salts
- Other drugs – allopurinol, iodides and radiocontrast media, interferon-α, omeprazole, penicillamine, tetracycline
- Tumour necrosis factor antagonists such as infliximab, etanercept and adalimumab[50]
- Imatinib mesylate (tyrosine kinase inhibitor)[51]
- Misoprostol (prostaglandin E1 agonist)

- Sildenafil citratus[52]
- Vaccines.[53]

Drugs that have been taken by the patient over the last 2 years prior to the onset of the exanthem have been considered to be the potential cause of the disease.

9. Ocular LP. A very rare variant of LP, which is usually seen in conjunction with skin or mucosal involvement. It is manifested as conjunctivitis, keratoconjunctivitis,[54] corneal ulceration and canalicular duct scarring.
10. Aural and urethral LP. Also rare variants of LP.

COMPLICATIONS

Acute complications: Itching is most common in cutaneous LP. In oral LP, eating might be so painful that patients are unable to maintain adequate nutrition. Oral lichen planus and the drugs used for the treatment may predispose to infection from *C. albicans.* Also *s*exual dysfunction may appear, which can also become a long-term complication in genital erosive lichen planus.

Chronic complications: After the lesions of lichen planus are resolved, the affected area of skin has a post-inflammatory hyperpigmentation, which is more noticeable in people with darker skin. Oral lichen planus can be very painful and ulceration may lead to scarring. Appendageal lichen planus can lead to scarring, while alopecia and nail loss are often permanent.

Cancer: Squamous cell carcinoma may arise from mucosal lesions (mouth, vulva, penile) and hypertrophic LP lesions (distal extremities).

A 1% incidence of SCC has been reported among patients with oral lichen planus.[3] Proposed reasons for the increased risk include the following:

- The oral mucosa affected by oral lichen planus may be more sensitive to *C. albicans* and to the exogenous mutagens found in tobacco and alcohol.

- In patients with oral lichen planus, the chronic inflammatory response and simultaneous healing response of epithelial wounds may increase the likelihood of cancer-forming gene mutations.

Case reports of SCC emerging from hypertrophic cutaneous LP lesions or chronic anogenital or esophageal lesions have been described.[3] Persistent ulcers/lesions should undergo biopsy, particularly when resistant to therapy.

Systemic complications: Infections, osteoporosis, adrenal insufficiency, bone marrow suppression, renal damage, hyperlipidemia may occur due to medication.

THERAPEUTIC MANAGEMENT

OBJECTIVES

Lichen planus is a chronic disease and the primary focus of treatment is to control symptoms and minimize damage. The treatment should be associated with the severity of the disease and the less possible side-effects and should improve the patients' quality of life.

In these guidelines, we give recommendations about treatment modalities of the various forms of LP trying to achieve the highest author's consensus level in the order of preference. All the drugs, except topical steroid preparations, constitute off-label treatment modalities.

Management of cutaneous lichen planus

The aim of the management of cutaneous lichen planus is to reduce itching and shorten the duration between onset of the disease and resolution of the lesions.
Topical glucocorticoids are the treatment of choice, although their efficacy has not been proven in well designed, randomized, controlled trials. When topical glucocorticoids are ineffective oral corticosteroids are administered. Oral corticosteroids are also preferred from the beginning of treatment, when atrophic lesions appear early in the evolution of the disease.

First line treatments

The first line treatments are summarized in table 4.

Table 4.
The following interventions are recommended for the treatment of cutaneous Lichen Planus
Topical steroids (superpotent and potent such as triamcinolone acetonide, fluocinolone acetonide, betamethasone dipropionate, and clobetasol propionate) or **Triamcinolone** intralesional injection, especially for more hypertrophic or unresponsive lesions, (5-20mg/ml every 2-4 weeks) [54]
Systemic corticosteroids (oral or intramuscular injections) If lesions are unresponsive to topical treatment oral prednisone of 30–80 mg/day for 4–6 weeks or intramuscular injections of triamcinolone 40–80 mg every 6–8 weeks are administered.[55,56]
Acitretin 20-35 mg/d, or isotretinoin [57,58,59]
Oral Cyclosporine (3-5 mg/kg/d) [60]

Symptomatic Treatment

Oral Antihistamines. Sedating antihistamines can be more effective in severe pruritus, but the reported adverse reports (safety problems / sleep disturbance / accidents), minimize their use.

Topical antipruritic agents: menthol, camphor, doxepin, polidocanole, etc. can be prescribed as an adjuvant to the main treatment.

Second line treatments

Although numerous treatment modalities exist, the physician should consider the benefits of the prescribed therapy against the possible side effects, because cutaneous LP is a self-limited disease with very few complications.

The second line treatments are summarized in the following table (5).

Table 5.
The following interventions are suggested for the treatment of cutaneous Lichen Planus
Broadband or Narrowband UVB. [63,64]
Combination of UV and acitretin
Topical calcineurin inhibitors (tacrolimus, pimecrolimus- twice/day for 1-2 months) [61]
Sulfasalazine, initial dose of 1.5g/d increased by 0.5g/week to 3g/d for 4-16 weeks [11,62]

The third line treatments are summarized in the following table (6).

Table 6.
The following interventions can be considered for the treatment of cutaneous Lichen Planus
Topical calcipotriol ointment [65]
Metronidazole[66] (250mg every 8hours for 12 weeks)
Trimethoprim-sulfomethoxazole
Hydroxychloroquine sulfate[11] (200-400mg/d)
Itraconazole[67], Terbinafine[68], Griseofulvin (why antifungal therapy is sometimes effective in LP remains to be elucidated)
Tetracycline[69], Doxycycline
Mycophenolate mofetil (0.5 g twice daily for four weeks, then 1 g twice daily for at least 20 weeks)[70]
Azathioprine (50mg twice daily orally or 1- 2mg/kg/day, for a period varying from 3 to 7 months)[71]

Methotrexate (15-20mg/week for 4-15 weeks) [72]
Cyclophosphamide[73] (50-100mg/d for 3-6 months)
Thalidomide[74]
Adalimumab[75]
Interferon a2b. Interesting approach especially if lichen planus is associated with hepatitis C.[76]
Alitretinoin[77]
Low molecular weight heparin (enoxaparin 3mg/week)[78]
Photodynamic therapy[79]
Extracorporeal photochemotherapy[80]
Nd-YAG laser, Low dose 308nm excimer laser[81]
Apremilast[82]
Ustekinumab [83]

Management of mucosal-oral LP.

Mucosal LP is often difficult to treat, particularly when ulcerations and erosions are present. For many years, treatment modalities for mucosal LP had been aimed at palliation rather than cure of oral symptoms. [84,85,86] However, current treatments should intend to the elimination of symptoms and potentially reduce the risk of malignant transformation.

General measures

Based on studies and expert opinions, measures of general care can be discussed before the onset and during the treatment. Patients should be advised of the need to maintain good oral hygiene and to avoid mucosal trauma. Depending on the severity of the disease, regular personal and professional dental care, replacement of amalgam or gold dental restorations[87], avoidance of smoking, spicy food and alcohol maybe indicated for some patients with oral lichen planus.[6,7]

If the cause of oral lichenoid lesions is suspected to be a systemic drug, (table 3) the physician should change the implicated drug to another medication.

There is some evidence to suggest that stress and anxiety are possible risk factors for the development of oral lichen planus (OLP). However, this association remains controversial.[88] It is assumed that psychological support may be beneficial to some patients with recurrent oral lichen planus. In case mucosal lesions persist despite treatment, frequent biopsies are necessary to exclude malignant transformation.

Management of oral LP

First line treatments

Topical application of potent or ultra-potent steroids is the mainstay of treatment in the case of localized OLP. Clobetasol propionate 0.05%, triamcinolone, betamethasone, fluocinonide, fluticasone, dexamethasone and prednisolone in different forms have been proved to be effective and safe. [89] They can be applied topically either in Orabase® or as lozenges. They have been also used as an ointment, as an oral suspension or aqueous solution, pellets, aerosol or spray, mouthwashes and usually in an adhesive paste. The frequency of application and the duration of maintenance treatment is a topic of discussion. Usually, twice daily application of topical steroids for 1-2 months, and then administered as needed, is a common practice.

Intralesional injection of corticosteroids (triamcinolone acetonide hydrocortisone, dexamethasone, and methylprednisolone) in ulcerative OLP is also an effective treatment approach.[89,90] Injections can be painful; to avoid mucosal atrophy we usually administer a corticosteroid dilution of 10 mg/mL.

Systemic corticosteroids, methylprednisolone or prednisone (30-80 mg/day) are the most effective treatment modality for patients with diffuse recalcitrant erosive OLP or multi-site

lesions of severe erosive OLP. This should be used in short burst to induce remission rather than as a long term maintenance therapy.

Systemic retinoids, such as acitretin (25-50mg/d) initially, followed by isotretinoin (0.5-1 mg/kg/d), have been used in the treatment of OLP. Topical retinoids (isotretinoin 0,05-0,1%) or other forms of vitamin A derivatives can eliminate white lesions, but in all cases reported the lesions relapsed 2-5 weeks after discontinuation of treatment.[91]

Systematic use of Cyclosporine (3-10 mg/kg/d) has been found to be effective in different studies and for some authors is considered to be the drug of choice. Topical cyclosporine was used in the form of mouthwashes or adhesive base, 2-3 times daily for 1 month. However the application of cyclosporine solution proved to be less effective than the application of clobetasol or triamcinolon acetonide, with no significant differences between the two treatments. Furthermore a large patient to patient variability regarding the efficacy of topical cyclosporine was observed in both studies. [92,93]

The first line treatments are summarized in the following table (7).

Table 7.
The following interventions are <u>recommended</u> for the treatment of mucosal Lichen Planus
Topical steroids (Clobetasol propionate 0.05%, triamcinolone, betamethasone, fluocinonide, fluticasone, dexamethasone and prednisolone in different forms). Intralesional injection of corticosteroids (triamcinolone acetonide hydrocortisone, dexamethasone, and methylprednisolone) in ulcerative OLP.
Systemic corticosteroids (oral) Systemic corticosteroids, methylprednisolone or prednisone (30-80mg/day)
Systemic retinoids, such as acitretin (25-50mg/d) initially, followed by isotretinoin (0.5-1mg/kg/d),

Topical retinoids (isotretinoin 0,05-0,1%) or other forms of vitamin A derivatives can eliminate white lesions,
Oral Cyclosporine (3-10mg/kg/d)

Second line treatments

In OLP recalcitrant to topical corticosteroids the use of topical calcineurin inhibitors, tacrolimus and pimecrolimus, is suggested.[61,94] Twice daily application for 4-6 weeks has been proven safe and efficacious.[61,94,95]

In few patients treated with topical calcineurin inhibitors, transformation in squamous cell carcinoma has been described, but it is not clear if it can be attributed to the medications applied or to the disease or to any other reason.[96,97,98]

The second line treatments are summarized in the following table (8).

Table 8.
The following interventions are <u>suggested</u> for the treatment of mucosal Lichen Planus
1. Topical calcineurin inhibitors, tacrolimus and pimecrolimus
2. Sulfasalasine[99] (2.5 g/day for 6 weeks)
3. Azathioprine [71,100](50mg twice daily orally or 1- 2mg/kg/day, for a period varying from 3 to 7 months)
4. Hydroxychloroquine sulfate [101] (200-400mg/d for 2 months)
5. Methotrexate[102] (15mg/week for 3 months)
6. Mycophenolate mofetil[103] (1 to 3g/daily twice daily for 4 weeks,)
7. TNF-a inhibitors (Alefacept, Adalimumab, Etanercept) [104,105,106] can be used with uncertain efficacy, because studies of large series of patients are lacking.

Third line treatments

The third line treatments are summarized in the following table (9).

Table 9.
The following interventions can be considered for the treatment of mucosal Lichen Planus
Cyclophosphamide (100 mg/d),[107]
Thalidomide[108] (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-[109], Trimethoprim-sulfomethoxazole, Tetracycline 500mg twice daily, Doxycycline 100mg twice daily),[110]
Itraconazole[111], Griseofulvin,[112]
Dapsone (initial dose of 50 mg/day is given for the first 15 days and then the dose is increased to 100mg/d),[113]
Low molecular weight heparin (enoxeparin 3mg/week),[114]
Interferon has been used as a treatment modality in cases of LP associated with hepatitis C [115]
Levamizole (50 mg thrice daily or 150mg once daily, for three consecutive days per week for at least 3 months),[116]
Lycopene (8 mg/day of for 8 weeks),[117]
Purslane (235mg/day),[118]
Curcuminoids (6000 mg/d 3 divided doses),[119]
Topical tocoferol [120]
Colchicine[121]
0.5ml of intralesional BCG (bacillus Calmette-Guerin) injection[122] 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 photochemotherapy[123]
Psoralen plus UVA (PUVA), UVA_1, Broadband or Narrowband UVB [124]
Er: YAG laser (2940nm),[125] diode laser (630nm),[126] Carbon dioxide laser (CO_2)[127]

In the most recent Cochrane review (2012) authors suggested that there is only weak evidence for the effectiveness of any of the treatments for oral erosive LP.[7]

Management of genital LP (table 10).

The general principles of the management of genital LP are similar with those of the LP confined to the oral mucosa. [128]We will discuss briefly some additional therapeutic measures. Also most cases of papulosquamous genital LP are self limited and treatment with emollient and mid potency steroids for a few weeks, is only required.

Prevention or limitation of scarring is the major therapeutic aim for erosive genital lesions of LP. In women synechiae formation with vaginal stenosis may be prevented by the use of vaginal dilators and vaginal steroids to treat mucosal inflammation; in uncircumcised men foreskin retraction is usually recommended to avoid phimosis. In rare cases, surgery may be needed to breakdown vaginal adhesions and phimosis to restore sexual functions.

Local anaesthetic gel, sedating antihistamines, low dose tricyclic antidepressants or anticonvulsants may prevent scratching and ease discomfort. Hydrocortisone acetate 25mg rectal suppositories can be inserted in the vagina nightly, or 1 gr clobetasol or another potent topical corticosteroid ointment can be inserted with an applicator to minimize scar formation.[129]

Our suggestion is to start with clobetasol or a calcineurin inhibitor and maintain the treatment with a less potent topical steroid, applied less frequently.

Long-term follow-up is necessary to monitor disease activity and to exclude malignant transformation of the erosive lesions.

Table 10.

The following interventions are recommended for the treatment of genital Lichen Planus
Topical steroids (hydrocortisone acetate 25mg rectal suppositories can be inserted in the vagina nightly, or 1 gr clobetasol or another potent topical corticosteroid ointment)
The following interventions are suggested for the treatment of genital Lichen Planus
A calcineurin inhibitor, tacrolimus – pimecrolimus
Local anaesthetic gel, sedating antihistamines, low dose tricyclic antidepressants or anticonvulsants

Management of appendageal LP

Lichen planopilaris

The aim of the treatment is the reduction of itching, burning and cessation of scarring. If the disease can be controlled in early stages, hair follicular units may be preserved and hairs can regrow.

First line treatments (table 11)

Topical steroids (superpotent, potent, mild) are the medication most frequently used in the management of LPP. [13, 130,131,132] They are sometimes effective and easily to apply to widespread lesions. However, most of the authors believe that their use is of doubtful value. Intralesional injection of corticosteroids (eg. triamcinolone 5-20mg/ml every 2-4 weeks) into localized lesions could be more efficacious in most cases. [133]

Systemic steroids (30-80mg/day of prednisone equivalent) are administered especially if the disease is rapidly progressive leading to severe scarring. [134]

It has been suggested by a systematic review of the literature and supported by experts' opinion that cyclosporine in systemic administration (3-10mg/kg/d) maybe an effective drug in appendageal LP.[135, 136]

Several studies investigated the efficacy of Hydroxychloroquine in lichen planopillaris have been published.

The efficacy of methotrexate has been studied in a randomized clinical trial comparing hydroxychloroquine (400 mg daily) versus methotrexate (15 mg weekly) administered for 6 months. Methotrexate showed significant improvement in all the assessed variables.[140]

The use of topical calcineurin inhibitors, primarily tacrolimus (twice daily for at least one month), either as monotherapy, or as an adjuvant to systemic therapy has been suggested in the management of LPP. [138]

Table 11.
The following interventions are <u>recommended</u> for the treatment of appendageal Lichen Planus
Topical steroids (superpotent, potent, mild)
Intralesional injection of corticosteroids (eg. triamcinolone 5-20mg/ml every 2-4 weeks)
Systemic steroids (30-80mg/day of prednisone)
Cyclosporine in systemic administration (3-10mg/kg/d)
Hydroxychloroquine sulfate (200-400mg/d or 6.5 mg/kg per day for 6 to 12 months)[132,137,139]
Methotrexate (15 mg/weekly for 6 months)[140]
Topical calcineurin inhibitors, primarily tacrolimus[138]

Second line treatments

The following medications have been proposed as second line therapies in the management of LPP, according to the highest author's consensus level in the order of preference (table 12):

Table 12.
The following interventions are <u>suggested</u> for the treatment of appendageal

Lichen Planus
Systemic retinoids such as acitretin (25-30mg/d) and isotretinoin (0,5-1mg/kg/d) for 3-6 months, especially in cases with pronounced perifollicular hyperkeratosis. [132,133]
Tetracycline / Doxycycline (100mg/d for one month)[129,133]
Mycophenolate mofetil (0.5 g twice daily for four weeks, then 1 g twice daily for at least 20 weeks) [129,136,139,141]
Adalimumab, at the same dose and schedule as in psoriasis[142]
Pioglitazone, an oral PPAR-γ agonist (15 mg orally once a day for 8 months)[143,144]
Minoxidil solution 5% [133]
Thalidomide (Initial dose 100 to 300 mg per day)[145,146]
Rituximab (IV 375 mg/m^2 once weekly for 4 or 8 doses)[147]
308nm excimer laser[148]

Frontal Fibrosing Alopecia

Treatment modalities for FFA include all medications described for the treatment of LPP. However, several authors believe that oral cyclosporine (3-6 mg/Kg/d)[135] and oral finasteride (2, 5 mg daily) or dutasteride (0.5 mg daily) for 12 months could be of considerable value.[149,150]However, since the co-existence of FFA and androgenetic alopecia is very common the effect of finasteride/dutasteride in FFA is doubtful.

Topical minoxidil or intralesional corticosteroids have been prescribed more often as an adjuvant to the previous treatments, depending on the stage of the disease and association to androgenetic alopecia. [151,152,153]

Nail lichen planus

Ungual LP is generally difficult to treat. Prognosis of this disease subtype is poor, with a high rate of recurrences. Treatment should be implemented immediately to prevent irreversible

changes, like pterygium, or total nail loss. About 50% of the patients will not be cured, despite any treatment. [154]

As first line treatment, triamcinolone acetonide injections 0.5mg/kg IM every 30 days can be used and then tapered off for isolated nail involvement. Also intralesional injections of triamcinolone acetonide 0.5-0.1mg/nail every 2 months seem to be effective but painful. Oral prednisone 0.5mg/Kgr for 3 weeks demonstrated a marked improvement and is useful when multiple nails are affected.[154, 155]

Topical steroids applied to the involved sites, especially in occlusive dressing, appear to have good results in some patients.

The following treatment modalities (table 13) can be considered as an alternative therapy to steroids[155,156]

Table 13.
Alitretinoin (30mg once a day for 3-6 months)[156,157]
Chloroquine phosphate (250mg twice daily for 10-30 weeks)[154]
Cyclosporine (3mg/kgr for several months)[158]
Acitretin [159]
Tacrolimus ointment 0.1% twice daily for 6 months[160]
5% Fluorouracil applied topically[154]
Biotin 2.5mg (children) and 7.5-10mg (adults) daily for 6 months[154]
Etanercept (25 mg sc. twice weekly for the first 6 months and 50 mg sc. once weekly thereafter)[161]

Other forms of LP

The treatment of other forms of LP is symptomatic and depends on the location of that lichenoid reaction on skin or mucosal according to the above suggestions.

In these guidelines the authors express their expert opinion based on their clinical Knowledge and review of the literature, authors and publishers cannot take responsibility for dosages and therapeutic choices, as therapy of lichen planus may change between cycles

of the guideline. Therefore the use of this guideline is at the physician's responsibility and users are requested to keep informed about new knowledge published in parallel to the guidelines. The authors and publishers of the guideline would be grateful if readers could inform them of any inaccuracies.

Acknowledgements

The guidelines are produced on behalf of the following organizations: the European Academy of Dermatology and Venereology (EADV); the European Dermatology Forum (EDF).

REFERENCES

1. Kanwar AJ, De D. Lichen planus in children. Indian J Dermatol Venereol Leprol 2010;76:366-72.
2. Giuliani M, Troiano G, Cordaro M, Corsalini M, Gioco G, Lo Muzio L, Pignatelli P, Lajolo C. Rate of malignant transformation of oral lichen planus: A systematic Oral Dis. 2018 May 8. doi: 10.1111/odi.12885
3. Le Cleach, L. and O. Chosidow. Clinical practice. Lichen planus. N Engl J Med, 2012; 366(8):723-32.
4. McCartan, B.E. and C.M. Healy. The reported prevalence of oral lichen planus: a review and critique. J Oral Pathol Med, 2008; 37(8): 447-53.
5. Friedl TK, Flaig MJ, Ruzicka T, Rupec RA. Verrucous squamous cell carcinoma complicating hypertrophic lichen planus. Three case reports and review of the literature. Hautarzt. 2011;62(1):40-5.
6. Thongprasom K., Carrozzo M, Furness S, Lodi G. Interventions for treating oral lichen planus. Cochrane Database Syst Rev, 2011 Jul 6;(7).
7. Cheng, S., Kirtschig G, Cooper S, et al., Interventions for erosive lichen planus affecting mucosal sites. Cochrane Database Syst Rev, 2012 Feb 15;2.
8. García-Pola MJ, González-Álvarez L, Garcia-Martin JM. Treatment of oral lichen planus. Systematic review and therapeutic guide. Med Clin (Barc). 2017: 23; 149(8):351-362
9. Antiga E Caproni M, Parodi A, Cianchini G, Fabbri P : Treatment of cutaneous lichen planus: an evidence based analysis of efficacy by the Italian Group for Cutaneous Immunopathology G Ital Dermatol Venereol. 2014;149(6):719-26.
10. Fazel N. Cutaneous lichen planus: A systematic review of treatments. J Dermatol Treat 2015;26(3):280-3.

11.Cribier B, Frances C, Chosidow O. Treatment of lichen planus. An evidence-based medicine analysis of efficacy. Arch Dermatol 1998; 134: 1521–1530.

12. Atzmony L, Reiter O, Hodak E, Gdalevich M, Mimouni D. Treatments for Cutaneous Lichen Planus: A Systematic Review and Meta-Analysis. Am J Clin Dermatol. 2016;17(1):11-22

13. Errichetti E, Figini M, Croatto M, Stinco G. Therapeutic management of classic lichen planopilaris: a systematic review. Clin Cosmet Investig Dermatol. 2018:27;11:91-102

14.Pittelkow MR, Daoud MS. Lichen planus. In: Wolff GK, Goldsmith L, Katz S, Gilchrest B, Paller A, eds. Fitzpatrick's Dermatology in general medicine. 7th ed. New York: Mc-Graw-Hill, 2008:244-55.

15.Wenzel J, Tuting T. An IFN-associated cytotoxic cellular immune response against viral, self-, or tumor antigens is a common pathogenetic feature in “interface dermatitis.” J Invest Dermatol 2008;128(10):2392-402.

16. Ma J, Zhang J, Zhang Y, Lv T, Liu J. The Magnitude of the Association between Human Papillomavirus and Oral Lichen Planus: A Meta-Analysis. PLoS One. 2016 Aug 29;11

17. Nahidi Y, Tayyebi Meibodi N, Ghazvini K, Esmaily H, Esmaeelzadeh M. Association of classic lichen planus with human herpesvirus-7 infection. Int J Dermatol. 2017 Jan;56(1):49-53

18. Choi YS, Kim Y, Yoon HJ, Baek KJ, Alam J, Park HK, Choi Y. The presence of bacteria within tissue provides insights into the pathogenesis of oral lichen planus. Sci Rep. 2016:7;6:29186

19. Li D, Li J, Li C, Chen Q, Hua H. The Association of Thyroid Disease and Oral Lichen Planus: A Literature Review and Meta-analysis. Front Endocrinol (Lausanne). 2017 Nov 9;8:310

20. Otero Rey EM, Yáñez-Busto A, Rosa Henriques IF, López-López J, Blanco-Carrión A. Lichen planus and diabetes mellitus: Systematic review and meta-analysis. Oral Dis. 2018 Sep 11. doi: 10.1111/odi.12977

21.Arias-Santiago S, Buendia-Efsman A, Aneiros-Fernandez J, ey al. Cardiovascular risk factors in patients with lichen planus. Am J Med 2011;124:543-8.

22. Shengyuan, L., Songpo, Y., Wen, W., Wenjing, T., Haitao, Z., Binyou, W. Hepatitis C virus and lichen planus: a reciprocal association determined by a meta-analysis. Arch Dermatol 2009:145;1040-1047.
23. Carrozzo M, Pellicano R. Lichen planus and hepatitis C virus infection: an updated critical review. Minerva Gastroenterol Dietol. 2008;54(1):65-74.
24. Jang SH, Yun SJ, Lee SC, Lee JB. Lichen planus pemphigoides associated with chronic hepatitis B virus infection. Clin Exp Dermatol. 2015;40(8):868-71.
25. Tarakji B, Ashok N, Alakeel R, et al. Hepatitis B vaccination and associated oral manifestations: a non-systematic review of literature and case reports. Ann Med Health Sci Res 2014;4(6):829-36.
26. Remmerbach TW, Liese J, Krause S, et al.No association of oral lichen planus and hepatitis C virus infection in central Germany. Clin Oral Investig. 2016;20(1):193-7.
27. Gheorghe C, Mihai L, Parlatescu I, Tovaru S. Association of oral lichen planus with chronic C hepatitis. Review of the data in literature. Maedica (Buchar).2014;9(1):98-103.
28. Birkenfeld S, Dreiher J, Weitzman D, Cohen AD. A study on the association with hepatitis B and hepatitis C in 1557 patients with lichen planus. J Eur Acad Dermatol Venereol 2011;25(4):436-40.
29. Gorouhi F, Davari P, Fazel N. Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal. 2014;2014:742826.
30. Weedon D. Weedon's Skin Pathology. 3rd Edition, London, Churchill Livingstone Elsevier 2010, pages 36-45.
31. Ioannides D, Bystryn JC. Immunofluorescence abnormalities in lichen planopilaris. Arch Dermatol. 1992;128(2):214-6.
32. Kulthanan K, Jiamton S, Varothai S, et al. Direct immunofluorescence study in patients with lichen planus. Int J Dermatol 2007; 46: 1237–1241.
33. Vazquez-Lopez F, Gomez-Diez S, Sanchez J, et al. Dermoscopy of active lichen planus. Arch Dermatol 2007;143:1092.
34. Lallas A, Kyrgidis A, Tzellos TG, et al. Accuracy of dermoscopic criteria for the diagnosis of psoriasis, dermatitis, lichen planus and pityriasis rosea. Br J Dermatol. 2012;166(6):1198-205.

35. Lehman J S, Tollefson M., Gibson L E., Lichen planus. International Journal of Dermatology 2009;48:682–694
36. Yiannias JA, el-Azhary RA, Hand JH, *et al*. Relevant contact sensitivities in patients with the diagnosis of oral lichen planus. J Am Acad Dermatol 2000;42: 177–182.
37. Kossard S. Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution. Arch Dermatol. 1994;130(6):770-4.
38. Kirtschig G, Wakelin SH, Wojnarowska F. Mucosal vulval lichen planus: outcome, clinical and laboratory features. J Eur Acad Dermatol Venereol. 2005;19(3):301-7.
39. The British Society for Oral Medicine. Guidelines for the Management of oral lichen planus in Secondary Care. October 2010.
40. RC Simpson, KS Thomas, P Leighton, R Murphy. Diagnostic criteria for erosive lichen planus affecting the vulva: an international electronic-Delphi consensus exercise. Br J Dermatol. 2013; 169(2): 337–343
41. Edwards SK, Bates CM, Lewis F, Sethi G, Grover D. 2014 UK national guideline on the management of vulval conditions. Int J STD AIDS. 2015;26(9):611-24.
42. Machin SE, McConnell DT, Adams JD. Vaginal lichen planus: preservation of sexual function in severe disease. BMJ Case Rep. 2010;2010.
43. Halevy S, Shai A. Lichenoid drug eruptions. J Am Acad Dermatol 1993; 29: 249–255.
44. Clayton R, Chaudhry S, Ali I, Cooper S, Hodgson T, Wojnarowska F. Mucosal (oral and vulval) lichen planus in women: are angiotensin-converting enzyme inhibitors protective, and beta-blockers and non-steroidal anti-inflammatory drugs associated with the condition? Clin Exp Dermatol. 2010;35(4):384-7.
45. Thompson DF, Skaehill PA. Drug-induced lichen planus. Pharmacotherapy. 1994;14:561–571.
46. Viñas M, Castillo MJ, Hernández N, Ibero M. Cutaneous drug eruption induced by antihistamines. Clin Exp Dermatol. 2014;39(8):918-20.
47. Artico G, Bruno IS, Seo J, Hirota SK, Acay R, Migliari DA. Lichenoid reaction to carbamazepine in the oral mucosa: case report. An Bras Dermatol. 2011;86(4 Suppl 1):S152-5.
48. Frentz G, Wadskov S, Kassis V. Ethambutol-induced lichenoid eruption. Acta Derm Venereol. 1981;61(1):89-91.

49.Sudha R, Vetrichevvel TP, Krishnarathnam K, Anandan S. Imatinib induced lichen planus. Indian J Dermatol. 2011;56(3):351-2.

50.Asarch A, Gottlieb AB, Lee J, et al. Lichen planus-like eruptions: an emerging side effect of tumor necrosis factor-alpha antagonists. J Am Acad Dermatol. 2009 ;61(1):104-11.

51.Kuraishi N, Nagai Y, Hasegawa M, Ishikawa O. Lichenoid drug eruption with palmoplantar hyperkeratosis due to imatinib mesylate: a case report and a review of the literature. Acta Derm Venereol. 2010;90(1):73-6.

52.Goldman BD. Lichenoid drug reaction due to sildenafil. Cutis. 2000;65(5):282-3.

53.Kanwar AJ, De D. Lichen planus in childhood: report of 100 cases. Clin Exp Dermatol. 2010;35(3):257-62.

54.Brewer JD, Ekdawi NS, Torgerson RR, et al. Lichen planus and cicatricial conjunctivitis: disease course and response to therapy of 11 patients. J Eur Acad Dermatol Venereol. 2011;25(1):100-4.

55.Volden G. Successful treatment of chronic skin diseases with clobetasol propionate and a hydrocolloid occlusive dressing. Acta Derm Venereol 1992; 72: 69–71.74

56.Malhotra AK, Khaitan BK, Sethuraman G, Sharma VK. Betamethasone oral minipulse therapy compared with topical triamcinolone acetonide (0.1%) paste in oral lichen planus: a randomized comparative study. J Am Acad Dermatol 2008;58:596-602

57.Laurberg G, Geiger JM, Hjorth N, *et al*. Treatment of lichen planus with acitretin. A double-blind,placebo-controlled study in 65 patients. J Am Acad Dermatol 1991; 24: 434–437

58.Handler HL. Isotretinoin for oral lichen planus. J Am Acad Dermatol 1984; 10: 674

59.Woo TY. Systemic isotretinoin treatment of oral and cutaneous lichen planus. *Cutis* 1985; 35: 385–6, 390–1, 393

60.Ho VC, Gupta AK, Ellis CN, Nickoloff BJ, Voorhees JJ. Treatment of severe lichen planus with cyclosporine. J Am Acad Dermatol. 1990;22(1):64-8

61.Samycia M, Lin AN. Efficacy of topical calcineurin inhibitors in lichen planus. J Cutan Med Surg. 2012;16(4):221-9.

62. Bauza A, Espana A, Gil P, et al. Successful treatment of lichen planus with sulfasalazine in 20 patients. Int J Dermatol 2005;44:158-62

63. Iraji F, Faghihi G, Asilian A, Siadat AH, Larijani FT, Akbari M. Comparison of the narrow band UVB versus systemic corticosteroids in the treatment of lichen planus: A randomized clinical trial. J Res Med Sci. 2011;16(12):1578-82
64. Alsenaid A, Alamri A, Prinz JC, Ruzicka T, Wolf R. Lichen planus of the lower limbs: successful treatment with psoralen cream plus ultraviolet A photochemotherapy Dermatol Therapy 2015 Dec 2. doi: 10.1111/dth.12321. [Epub ahead of print]
65. Theng CT, Tan SH, Goh CL, Suresh S, Wong HB, Machin D; Singapore Lichen Planus Study Group. A randomized controlled trial to compare calcipotriol with betamethasone valerate for the treatment of cutaneous lichen planus. J DermatologTreat. 2004;15(3):141-5.
66. Rasi A, Behzadi AH, Davoudi S, et al. Efficacy of oral metronidazole in treatment of cutaneous and mucosal lichen planus. J Drugs Dermatol. 2010;9(10):1186-90.
67.Khandpur S, Sugandhan S, Sharma VK. Pulsed itraconazole therapy in eruptive lichen planus. J Eur Acad Dermatol Venereol. 2009;23(1):98-101.
68. Click JW, Wilson BB. The use of oral terbinafine or topical ciclopirox for lichen planus. Cutis. 2009;84(1):42.
69. Hantash BM, Kanzler MH. The efficacy of tetracycline antibiotics for treatment of lichen planus: an open-label clinical trial. Br J Dermatol. 2007;156(4):758-60.
70. Manousaridis I, Manousaridis K, Peitsch WK, Schneider SW. Individualizing treatment and choice of medication in lichen planus: a step by step approach. J Dtsch Dermatol Ges. 2013; 11(10):981-91.
71. Verma KK, Sirka CS, Khaitan BK. Generalized severe lichen planus treated with azathioprine. Acta Derm Venereol. 1999;79(6):493
72. Turan H, Baskan EB, Tunali S, Yazici S, Saricaoglu H. Methotrexate for the treatment of generalized lichen planus. J Am Acad Dermatol. 2009;60(1):164-6.
73. Paslin DA. Sustained remission of generalized lichen planus induced by cyclophosphamide. Arch Dermatol. 1985;121(2):236-9
74. Moura AK, Moure ER, Romiti R. Treatment of cutaneous lichen planus with thalidomide. Clin Exp Dermatol. 2009;34(1):101-3.
75. Holló P, Szakonyi J, Kiss D, Jokai H, Horváth A, Kárpáti S. Successful treatment of lichen planus with adalimumab. Acta Derm Venereol. 2012;92(4):385-6

76. Lapidoth M, Arber N, Ben-Amitai D, Hagler J. Successful interferon treatment for lichen planus associated with chronic active hepatitis due to hepatitis C virus infection. Acta Derm Venereol. 1997;77(2):171-2
77. Molin S, Ruzicka T. Oral alitretinoin in lichen planus: two case reports. Acta Derm Venereol. 2010;90(5):523-4.
78. Iraji F, Asilian A, Saeidi A, Siadat AH, Saeidi AR, Hassanzadeh A. Comparison of therapeutic effect of low-dose low-molecular-weight heparin (enoxaparin) vs.oral prednisone in treatment of patients with lichen planus; A clinical trial. Adv Biomed Res. 2013;2:76.
79. Kirby B, Whitehurst C, Moore JV, Yates VM. Treatment of lichen planus of the penis with photodynamic therapy. Br J Dermatol. 1999;141(4):765-6.
80. Zingoni A, Deboli T, Savoia P, Bernengo MG. Effectiveness of extracorporeal photochemotherapy in the treatment of a case of refractory erosive lichen planus.J Dermatolog Treat. 2010;21(2):119-21.
81. Trehan M, Taylor CR. Low-dose excimer 308-nm laser for the treatment of oral lichen planus. Arch Dermatol. 2004;140(4):415-20.
82. Paul J, Foss CE, Hirano SA, Cunningham TD, Pariser DM. An open-label pilot study of apremilast for the treatment of moderate to severe lichen planus: a case series. J Am Acad Dermatol. 2013;68(2):255-61.
83. Knisley RR, Petropolis AA, Mackey VT. Lichen planus pemphigoides treated with ustekinumab. Cutis. 2017;100(6):415-418.
84. Chan ES, Thornhill M, Zakrzewska J. Interventions for treating oral lichen planus. Cochrane Database Syst Rev. 2000 (2):CD001168.
85. Eisen D. The therapy of oral lichen planus. Crit Rev Oral Biol Med. 1993;4(2):141-58.
86. McCartan B, McCreary C. What is the rationale for treating oral lichen planus? Oral Dis. 1999;5(3):181-2.
87. Henriksson E, Mattsson U, Hakansson J. Healing of lichenoid reactions following removal of amalgam. A clinical follow-up. J Clin Periodontol. 1995; 22:287–294.
88. Vallejo MJ(1), Huerta G, Cerero R, Seoane JM. Anxiety and depression as risk factors for oral lichen planus. Dermatology 2001;203(4):303-7.

89. Carbone M, Goss E, Carrozzo M, et al. Systemic and topical corticosteroid treatment of oral lichen planus: a comparative study with long-term follow-up. J Oral Pathol Med. 2003;32(6):323-9.
90. Silverman S Jr, Gorsky M, Lozada-Nur F, Giannotti K. A prospective study of findings and management in 214 patients with oral lichen planus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1991; 72:665-70.
91. Giustina TA, Stewart JC, Ellis CN, et al. Topical application of isotretinoin gel improves oral lichen planus. Arch Dermatol 1986;122:534-536.
92. Yoke PC, Tin GB, Kim MJ, et al; Asian Lichen Planus Study Group. A randomized controlled trial to compare steroid with cyclosporine for the topical treatment of oral lichen planus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;102(1):47-55.
93. Conrotto D, Carbone M, Carrozzo M, et al. Ciclosporin vs. clobetasol in the topical management of atrophic and erosive oral lichen planus: a double-blind, randomized controlled trial. Br J Dermatol. 2006;154(1):139-45
94. Shilpa PS, Kaul R, Bhat S, Sanjay CJ, Sultana N. Topical tacrolimus in the management of oral lichen planus: literature review. J Calif Dent Assoc. 2014;42(3):165-70.
95. McCaughey C, Machan M, Bennett R, Zone JJ, Hull CM. Pimecrolimus 1% cream for oral erosive lichen planus: a 6-week randomized, double-blind, vehicle-controlled study with a 6-week open-label extension to assess efficacy and safety. J Eur Acad Dermatol Venereol. 2011;25(9):1061-7.
96. Mattsson U, Magnusson B, Jontell M. Squamous cell carcinoma in a patient with oral lichen planus treated with topical application of tacrolimus. Oral Surg OralMed Oral Pathol Oral Radiol Endod. 2010;110(1):e19-25.
97. Becker JC, Houben R, Vetter CS, Bröcker EB. The carcinogenic potential of tacrolimus ointment beyond immune suppression: a hypothesis creating case report.BMC Cancer. 2006;6:7.
98. Giuliani M, Troiano G, Cordaro M, Corsalini M, Gioco G, Lo Muzio L, Pignatelli P, Lajolo C. Rate of malignant transformation of oral lichen planus: A systematic Oral Dis. 2018 May 8. doi: 10.1111/odi.12885
99. Omidian M, Ayoobi A, Mapar MA, Feily A, Cheraghian B. Efficacy of sulfasalazine in the treatment of generalized lichen planus: randomized double-blinded clinical trial on 52 patients. J Eur Acad Dermatol Venereol. 2010;24(9):1051-4.

100. Verma KK, Mittal R, Manchanda Y. Azathioprine for the treatment of severe erosive oral and generalized lichen planus. Acta Derm Venereol. 2001;81(5):378-9.

101. Eisen D. Hydroxychloroquine sulfate (Plaquenil) improves oral lichen planus: An open trial. J Am Acad Dermatol. 1993;28(4):609-12.

102. Torti DC, Jorizzo JL, McCarty MA. Oral lichen planus: a case series with emphasis on therapy. Arch Dermatol. 2007;143(4):511-5.

103. Dalmau J, Puig L, Roé E, Peramiquel L, Campos M, Alomar A. Successful treatment of oral erosive lichen planus with mycophenolate mofetil. J Eur Acad Dermatol Venereol. 2007;21(2):259-60

104. Chang AL, Badger J, Rehmus W, Kimball AB. Alefacept for erosive lichen planus: a case series. J Drugs Dermatol. 2008;7(4):379-83.

105. Chao TJ. Adalimumab in the management of cutaneous and oral lichen planus. Cutis 2009;84(6):325-8

106. O'Neill ID. Off-label use of biologicals in the management of inflammatory oral mucosal disease. J Oral Pathol Med. 2008;37(10):575-81.

107. Paslin DA. Sustained remission of generalized lichen planus induced by cyclophosphamide. Arch Dermatol. 1985;121(2):236-9.

108. Wu Y, Zhou G, Zeng H, Xiong CR, Lin M, Zhou HM. A randomized double-blind, positive-control trial of topical thalidomide in erosive oral lichen planus. OralSurg Oral Med Oral Pathol Oral Radiol Endod. 2010;110(2):188-95.

109. Rasi A, Behzadi AH, Davoudi S, et al. Efficacy of oral metronidazole in treatment of cutaneous and mucosal lichen planus. J Drugs Dermatol. 2010;9(10):1186-90.

110. Hantash BM, Kanzler MH. The efficacy of tetracycline antibiotics for treatment of lichen planus: an open-label clinical trial. Br J Dermatol. 2007;156(4):758-60.

111. Khandpur S, Sugandhan S, Sharma VK. Pulsed itraconazole therapy in eruptive lichen planus. J Eur Acad Dermatol Venereol. 2009;23(1):98-101.

112. Naylor GD. Treating erosive lichen planus with griseofulvin: a report of four cases. Quintessence Int. 1990;21(12):943-7.

113. Beck HI, Brandrup F. Treatment of erosive lichen planus with dapsone. Acta Derm Venereol. 1986;66(4):366-7.

114. Hodak E, Yosipovitch G, David M, et al. Low-dose low-molecular-weight heparin (enoxaparin) is beneficial in lichen planus: a preliminary report. J Am Acad Dermatol. 1998;38(4):564-8
115. Lapidoth M, Arber N, Ben-Amitai D, Hagler J. Successful interferon treatment for lichen planus associated with chronic active hepatitis due to hepatitis C virus infection. Acta Derm Venereol. 1997;77(2):171-2.
116. Patil A, Prasad S, Ashok L, Sujatha GP. Oral bullous lichen planus: Case report and review of management. Contemp Clin Dent. 2012;3(3):344-8.
117. Saawarn N, Shashikanth MC, Saawarn S, Jirge V, Chaitanya NC, Pinakapani R. Lycopene in the management of oral lichen planus: a placebo-controlled study. Indian J Dent Res. 2011;22(5):639-43.
118. Agha-Hosseini F, Borhan-Mojabi K, Monsef-Esfahani HR, Mirzaii-Dizgah I,Etemad-Moghadam S, Karagah A. Efficacy of purslane in the treatment of oral lichen planus. Phytother Res. 2010;24(2):240-4.
119. Chainani-Wu N, Madden E, Lozada-Nur F, Silverman S Jr. High-dose curcuminoids are efficacious in the reduction in symptoms and signs of oral lichen planus. J Am Acad Dermatol. 2012;66(5):752-60.
120. Bacci C, Vanzo V, Frigo AC, Stellini E, Sbricoli L, Valente M. Topical tocopherol for treatment of reticular oral lichen planus: a randomized,double-blind, crossover study. Oral Dis. 2017 Jan;23(1):62-68.
121. Joyce Kou Ho; Basil M. Hantash. Systematic Review of Current Systemic Treatment Options for Erosive Lichen Planus: Results & Discussion, Released: 07/05/2012; http://www.medscape.org/viewarticle/766707
122. Xiong C, Li Q, Lin M, et al. The efficacy of topical intralesional BCG-PSN injection in the treatment of erosive oral lichen planus: a randomized controlled trial. J Oral Pathol Med. 2009;38(7):551-8.
123. Bécherel PA, Bussel A, Chosidow O, Rabian C, Piette JC, Francès C. Extracorporeal photochemotherapy for chronic erosive lichen planus. Lancet. 1998;351(9105):805.
124. Wackernagel A, Legat FJ, Hofer A, Quehenberger F, Kerl H, Wolf P. Psoralen plus UVA vs. UVB-311 nm for the treatment of lichen planus. Photodermatol Photoimmunol Photomed. 2007;23(1):15-9

125. Fornaini C, Raybaud H, Augros C, Rocca JP. New clinical approach for use of Er:YAG laser in the surgical treatment of oral lichen planus: a report of two cases. Photomed Laser Surg. 2012;30(4):234-8.
126. Misra N, Chittoria N, Umapathy D, Misra P. Efficacy of diode laser in the management of oral lichen planus. BMJ Case Rep. 2013 Mar 15;2013.
127. van der Hem PS, Egges M, van der Wal JE, Roodenburg JL. CO2 laser evaporation of oral lichen planus. Int J Oral Maxillofac Surg. 2008;37(7):630-3.
128. Cooper SM, Wojnarowska F. Influence of treatment of erosive lichen planus of the vulva on its prognosis. Arch Dermatol. 2006 Mar;142(3):289-94
129. Edwards L. Lichen planus. Chapter 15 in "Obstetric and Gynecologic Dermatology" eds Martin Black, C. Ambros-Rudolf, L. Edwards, P Lynch, Mosby Elsevier 2008;147-15.
130. Lajevardi V, Ghodsi SZ, Goodarzi A, Hejazi P, Azizpour A, Beygi S. Comparison of Systemic Mycophenolate Mofetil with Topical Clobetasol in Lichen Planopilaris: A Parallel-Group, Assessor- and Analyst-Blinded, Randomized Controlled Trial. Am J Clin Dermatol. 2015;16(4):303-11.
131. Chieregato C, Zini A, Barba A, Magnanini M, Rosina P. Lichen planopilaris: report of 30 cases and review of the literature. Int J Dermatol. 2003;42(5):342-5.
132. Lyakhovitsky A, Amichai B, Sizopoulou C, Barzilai A. A case series of 46 patients with lichen planopilaris: Demographics, clinical evaluation, and treatment experience. J Dermatolog Treat. 2015;26(3):275-9.
133. Cevasco NC, Bergfeld WF, Remzi BK, de Knott HR. A case-series of 29 patients with lichen planopilaris: the Cleveland Clinic Foundation experience on evaluation, diagnosis, and treatment. J Am Acad Dermatol. 2007;57(1):47-53.
134. Mehregan DA, Van Hale HM, Muller SA. Lichen planopilaris: clinical and pathologic study of forty-five patients. J Am Acad Dermatol. 1992;27(6):935-42.
135. Rácz E, Gho C, Moorman PW, Noordhoek Hegt V, Neumann HA. Treatment of frontal fibrosing alopecia and lichen planopilaris: a systematic review. J Eur Acad Dermatol Venereol. 2013;27(12):1461-70.
136. Assouly P, Reygagne P. Lichen planopilaris: update on diagnosis and treatment. Semin Cutan Med Surg 2009;28:3–10.

137. Spencer LA, Hawryluk EB, English JC 3rd. Lichen planopilaris: retrospective study and stepwise therapeutic approach. Arch Dermatol. 2009;145(3):333-4.
138. Blazek C, Megahed M. Lichen planopilaris. Successful treatment with tacrolimus. Hautarzt. 2008;59(11):874-7.
139. Chiang C, Sah D, Cho BK, Ochoa BE, Price VH. Hydroxychloroquine and lichen planopilaris: efficacy and introduction of Lichen Planopilaris Activity Index scoring system. J Am Acad Dermatol. 2010;62(3):387-92.
140. Naeini FF, Saber M, Asilian A, Hosseini SM. Clinical efficacy and safety of methotrexate versus hydroxychloroquine in preventing lichen planopilaris progress: a randomized clinical trial. Int J Prev Med. 2017;8:37
141. Cho BK, Sah D, Chwalek J, et al. Efficacy and safety of mycophenolate mofetil for lichen planopilaris. J Am Acad Dermatol.2010;62(3):393-7.
142. Kreutzer K, Effendy I. Therapy-resistant folliculitis decalvans and lichen planopilaris successfully treated with adalimumab. J Dtsch Dermatol Ges. 2014;12(1):74-6.
143. Mirmirani P, Karnik P. Lichen planopilaris treated with a peroxisome proliferator-activated receptor gamma agonist. Arch Dermatol 2009; 145:1363–1366.
144. Baibergenova A, Walsh S. Use of pioglitazone in patients with lichen planopilaris. J Cutan Med Surg. 2012;16(2):97-100.
145. George SJ, Hsu S. Lichen planopilaris treated with thalidomide. J Am Acad Dermatol. 2001;45(6):965-6.
146. Jouanique C, Reygagne P, Bachelez H, Dubertret L. Thalidomide is ineffective in the treatment of lichen planopilaris. J Am Acad Dermatol. 2004;51(3):480-1.
147. Erras S, Mouna Z, Akhdari N, Belaabidia B, Essaadouni L. Rapid and complete resolution of lichen planopilaris in juvenile chronic arthritis treated with rituximab. Eur J Dermatol 2011; 21: 116–117.
148. Navarini AA, Kolios AG, Prinz-Vavricka BM, Haug S, Trüeb RM. Low-dose excimer 308-nm laser for treatment of lichen planopilaris. Arch Dermatol. 2011;147(11):1325-6.
149. Vañó-Galván S, Molina-Ruiz AM, Serrano-Falcón C, et al. Frontal fibrosing alopecia: a multicenter review of 355 patients. J Am Acad Dermatol. 2014;70(4):670-8.

150. Georgala S, Katoulis AC, Befon A, Danopoulou I, Georgala C. Treatment of postmenopausal frontal fibrosing alopecia with oral dutasteride. J Am Acad Dermatol 2009; 61: 157–158.
151. Moreno-Ramírez D, Camacho Martínez F. Frontal fibrosing alopecia: a survey in 16 patients. J Eur Acad Dermatol Venereol. 2005;19(6):700-5.
152. MacDonald A, Clark C, Holmes S. Frontal fibrosing alopecia: a review of 60 cases. J Am Acad Dermatol. 2012;67(5):955-61.
153. Banka N, Mubki T, Bunagan MJ, McElwee K, Shapiro J. Frontal fibrosing alopecia: a retrospective clinical review of 62 patients with treatment outcome and long-term follow-up. Int J Dermatol. 2014;53(11):1324-30.
154. Baran R, Rigopoulos D. Lichen planus. In “Nail Therapies”, Informa Healthcare, London, UK 2012; pages 37-40.
155. Brauns B, Stahl M, Schön MP, Zutt M. Intralesional steroid injection alleviates nail lichen planus. Int J Dermatol. 2011;50(5):626-7.
156. Alsenaid A, Eder I, Ruzicka T, Braun-Falco M, Wolf R. Successful treatment of nail lichen planus with alitretinoin: report of 2 cases and review of the literature. Dermatology. 2014;229(4):293-6.
157. Iorizzo M. Nail lichen planus - a possible new indication for oral alitretinoin. J Eur Acad Dermatol Venereol. 2014 Dec 2 doi:10.1111/jdv.12904.
158. Florian B, Angelika J, Ernst SR. Successful treatment of palmoplantar nail lichen planus with cyclosporine. J Dtsch Dermatol Ges. 2014;12(8):724-5.
159. Alsenaid A, Lang A, Ruzicka T, Braun-Falco M, Wolf R. Lichen planus with associated myasthenia gravis-successful treatment with acitretin. Eur J Dermatol 2013 ;23(6):909-10.
160. Ujiie H, Shibaki A, Akiyama M, Shimizu H. Successful treatment of nail lichen planus with topical tacrolimus. Acta Derm Venereol. 2010;90(2):218-9.
161. Irla N, Schneiter T, Haneke E, Yawalkar N. Nail Lichen Planus: Successful Treatment with Etanercept. Case Rep Dermatol. 2010;2(3):173-176.

Table 2. Clinical variants	
Cutaneous LP	Localized cutaneous lesions of LP Generalized cutaneous LP Palmoplantar LP with localized erythematous scaly plaques Hypertrophic LP Atrophic LP Vesiculobullous LP Erosive and ulcerative LP Annular LP LP pigmentosus Lichen planus pemphigoides
Appendageal LP	Lichen planopilaris LP lesions of the nails
Mucosal LP	LP plaque-like or erosive Atrophic LP lesions of the oral mucosa Bullous LP of the mucosa Papular genital LP. Hypertrophic genital LP Chronic erosive LP lesions in genitalia Lichen planus of the esophagus
Other forms of LP	Invisible LP Overlap syndromes: LP erythematosus Lichenoid reaction of Graft-Versus-Host-Disease Lichenoid keratosis Drug-induced lichen planus Ocular LP Aural and urethral LP

Table 3. Drug-induced lichen planus	
Antihypertensive	ACE inhibitors, beta-blockers, nifedipine, methyldopa, diuretics (hydrochlorothiazide, furosemide, spironolactone, chlorothiazide)

Non-steroidal anti-inflammatory drugs (NSAIDs)	aspirin, diflunisal, ibuprofen, indomethacin, leflunomide, mesalamine, naproxen, rofecoxib, sulindac, sulfasalazine, tolbutamide
Metals	gold salts, arsenic
Anti-convulsants	carbamazapine, phenytoin, oxcarbazepine, valproate sodium
Drugs to treat tuberculosis	ethambutol, isoniazid, rifampicin
Antifungal drug	ketoconazole, amphotericin B, griseofulvin
Chemotherapeutic agents	hydroxyurea, 5-fluorouracil, imatinib, olmutinib
Antimalarial agents	hydroxychloroquine, chloroquine, pyrimethamine, quinidine, quinine
Sulfa drugs	sulfonylurea, hypoglycaemic agents, dapsone, mesalazine, sulfasalazine
Tumour necrosis factor antagonists	infliximab, etanercept and adalimumab
Other drugs	allopurinol, iodides and radiocontrast media, interferon-α, omeprazole, penicillamine, tetracycline, levamisole, clopidogrel, palifermin, mercapto-propionylglycine, misoprostol, nandrolene, furyl-propionate, norflex, omeprazole, pyrithioxin, sildenafil, tiopronin, isotretinoin, zidovudine, vaccines, solifenacin
Antidiabetics	chlorpropamide, glyburide, glipizide, insulin, tolazamide, tolbutamide
Antidiarrheals	bismuth
Lipid lowering drugs	gemfibrozil, orlistat, pravastatin, simvastatin
Psychiatric drugs	antipsychotics (chlorpromazine, levomepromazine, methopromazine, thioridazine), benzodiazepines (lorazepam), lithium, selective serotonin reuptake inhibitor (escitalopram), tricyclic antidepressants (amitriptyline, imipramine)