Elisabetta Botti

Linee guide europee lichen sclerosus

Lichen sclerosus

- ✓ Disordine infiammatorio cronico-recidivante mucoso-cutaneo genitale ed extragenitale
- ✓ Causa prurito, dolore bruciore, disparenuia, disfunzione sessuale
- ✓ LS anogenitale è associato ad un rischio maggiore di sviluppare SCC
- ✓ Distruzione delle strutture anatomiche
- ✓ Prevalenza del 0,1-3% 2 picchi di incidenza : prepuberale e post-menopausale
- ✓ Con rapporto femmine :maschi 3:1- 10:1

PATOGENESI : fattori genetici

- Il 12% delle donne affette da LSV presenta familiarità

- Associazione con HLA DQ7, DQ8, DQ9

(Sherman V, McPherson T, Baldo M, et al. The high rate of familial lichen sclerosus suggests a genetic contribution: an observational cohort study. J Eur Acad Dermatol Venereol. 2010;24:1031–4.

PATOGENESI : autoimmunità

- Il 21,5% delle pazienti ha una o piu' patologie autoimmuni
- Il 42% ha familiarità per patologie autoimmuni
- Il 42% presenta autoanticorpi

- autoanticorpi anti ECM1 nel siero del 74% delle donne affette vs il 7 % dei controlli

  (Oyama N, Chan I, Neill SM, et al. Autoantibodies to extracellular matrix protein 1 in lichen sclerosus. Lancet. 2003;362: 118–23.)

- Autoanticorpi anti BZM (BP180 e BP230 in un terzo delle pazienti

(Baldo M, Bailey A, Bhogal B, et al. T cells reactive with the NC16A domain of BP180 are present in vulval lichen sclerosus and lichen planus. J Eur Acad Dermatol Venereol. 2010;24: 186–90.

Baldo M, Bhogal B, Groves RW, et al. Childhood vulval lichen sclerosus: autoimmunity to the basement membrane zone protein BP180 and its relationship to autoimmunity. Clin Exp Dermatol. 2010;35:543–5.)

comorbidità

Le comorbidità piu’ comununi nelle donne (19-54%) che nei maschi (3-5%).

piu’ frequentemente associate sono:

Tiroiditi autoimmuni (12 %)
alopecia areata (9 %)
vitiligo (6 %)
Anemia perniciosa (2 %)

Comorbidities
Morphea or localized scleroderma
Systemic sclerosis
Hashimoto’s thyroiditis
Rheumatoid arthritis
Psoriasis
Diabetes mellitus type 1
Alopecia areata
Overactive bladder
Stress urinary incontinence
Irritable bowel syndrome
Fibromyalgia
Temporomandibular joint disorder

PATOGENESI : fattori ormonali

- Livelli sierici dimunuiti di diidrotestosterone nelle pazienti affetti *da LSV*

(Friedrich EG Jr, Kalra PS. Serum levels of sex hormones in vulvar lichen sclerosus, and the effect of topical testosterone. N Engl J Med. 1984;310:488–91.)

- diminuzione dell'espressione di recettori per androgeni nella cute lesionale delle pazienti affette

(Clifton MM, Garner IB, Kohler S, et al. Immunohistochemical evaluation of androgen receptors in genital and extragenital lichen sclerosus: evidence for loss of androgen receptors in lesional epidermis. J Am Acad Dermatol. 1999;41:43–6.)

- Studio caso-controllo 100 % delle pazienti affetti aveva utilizzato contracezzione orale vs il 66,4% dei controlli

(Gu¨nthert AR, Faber M, Knappe G, et al. Early onset vulvar lichen sclerosus in premenopausal women and oral contraceptives. Eur J Obstet Gynecol Reprod Biol. 2008;137:56–60.)

- Associazione con la S. di Turner (X0) , possibile influenza di bassi livelli di estrogeni.

(Koupaie J. Letter: Lichen sclerous et atrophicus associated with Turner syndrome. *Arch Dermatol*. Aug 1976)

SINTOMI

Symptoms

- Itch (mainly in genital LS in females)
- Pain / Soreness
- Burning
- Irritation
- Feeling of dryness
- Dysaesthesia
- Constipation, in perianal involvement, particularly in girls
- Dyspareunia or apareunia (disturbed sexual functioning)
- Dysuria (pain, disturbed urinary stream)
- Urinary bladder pain (abacterial cystitis)
- LS can be asymptomatic

Signs

- Oedema (swelling of the skin)
- Slight erythema (redness)
- Hyperkeratosis (white thickened skin; hyperkeratosis on histology)
- Sclerosis (tight, yellowish white skin, e.g. resulting in phimosis; dermal hyalinisation on histology)
- Pallor (pale, whitish areas; the histological correlate is not described)
- Atrophic skin (crinkly skin; epidermal atrophy on histology)
- Fissuring (skin fragility, loss of elasticity leading to splitting of skin)
- Erosions
- Blistering is very rare
- Ecchymoses / purpura is common in genital LS (due to fragile, sclerotic and ectatic blood vessels)
- Changes may be localised to the vulva or include the perianal area, forming a 'figure-of-eight' distribution
- Scarring may lead to architectural changes (e.g. resorption of the labia minora, fusing in the midline with burying, but not loss of the clitoris in women and e.g. phimosis, a narrow meatus urethrae and a sclerotic frenulum breve in men)
- Follicular plugging (in extragenital LS)

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Diagnosi differenziali:

- Inverse psoriasis
- eczema
- lichen simplex, non-specific balanoposthitis,
- vitiligo (particularly difficult in children),
- morphoea,
- graft versus host disease (GvHD),
- autoimmune bullous diseases,
- plasma cell vulvitis/balanitis,
- Paget disease, lSIL/hSIL and SCCs may show clinical features resembling LS.

Le sovrainfezioni e dermatite allergica possono associarsi successivamente

Version *[1], June 2023*

G Kirtschig[1], M Kinberger[2], A Kreuter[3], R Simpson[4], A Günthert[5], C van Hees[6], K Becker[7], MJ Ramakers[8], M Corazza[9], S Müller[10], S von Seitzberg[11], MJ Boffa[12], R Stein[13], G Barbagli[14], CC Chi[15,16], JN Dauendorffer[17], B Fischer[18], M Gaskins[2], E Hiltunen-Back[19], A Höfinger[18], NH Köllmann[18], H Kühn[20], HK Larsen[21] M Lazzeri[22], W Mendling[23], AF Nikkels[24], M Promm[25], KK Rall[26], S Regauer[27], M Sárdy[28], N Sepp[29], T Thune[30], A Tsiogka[31], S Vassileva[32], L Voswinkel[23], L Wölber[33], RN Werner[2]

the *guideline* development group is comprised of *34* experts from *17* countries, including *5* patient

Table 7: Wording of recommendations [10-13]

Strength	Wording	Symbols	Implications
Strong recommendation **for** the use of an intervention	'We **recommend** . . .'	↑↑	We believe that all or almost all informed people would make that choice. Clinicians will have to spend less time on the process of decision-making, and may devote that time to overcome barriers to implementation and adherence. In most clinical situations, the recommendation may be adopted as a policy.
Weak recommendation **for** the use of an intervention	'We **suggest** . . .'	↑	We believe that most informed people would make that choice, but a substantial number would not. Clinicians and health care providers will need to devote more time on the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making requires substantial debate.
No recommendation with respect to an intervention	'We **cannot make a recommendation** with respect to . . .'	**0**	At the moment, a recommendation in favour or against an intervention cannot be made due to certain reasons (e.g. no reliable evidence data available, conflicting outcomes, etc.)
Weak recommendation **against** the use of an intervention	'We **suggest against** . . .'	↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
Strong recommendation **against** the use of an intervention	'We **recommend against** . . .'	↓↓	We believe that all or almost all informed people would make a choice against that intervention. This recommendation can be adopted as a policy in most clinical situations.

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SCUOLA DERMATOLOGICA SERGIO CHIMENTI

8.1 Skin care and basic therapy

Recommendation	Strength	Consensus
We **recommend** the use of topical ointments instead of creams or gels in lichen sclerosus patients.	↑↑	>75% (11/12) Consensus-based
We **cannot make a recommendation** in favour of wearing silk rather than cotton briefs for lichen sclerosus patients.	0	100% 100 % Agreement (15/15) Consensus-based
We **suggest** avoidance of trigger factors (mechanical factors such as trauma, unnecessary surgical interventions, piercings) and irritants (excessive water exposure or cleansing products, synthetic and tight clothing, use of wet wipes, etc.) at the affected sites in lichen sclerosus patients.	↑	100% 100 % Agreement (15/15) Consensus-based
We **suggest** regular change of incontinence pads/absorbent pads and urine-soaked undergarments to maintain dry conditions as much as possible, as well as careful management of urine incontinence in lichen sclerosus patients.	↑	100% 100 % Agreement (15/15) Consensus-based
We **cannot make a recommendation** concerning the use of oral contraceptives in females with lichen sclerosus.	0	100% 100 % Agreement (14/14) Consensus-based

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8.2.1 Emollients

Recommendation	Strength	Agreement
We **recommend** co-treatment with topical emollients during standard therapy in women with genital lichen sclerosus.	↑↑	100% 100 % Agreement (17/17) Expert Consensus
We **recommend** co-treatment with topical emollients in girls with genital lichen sclerosus.	↑↑	
We **suggest** co-treatment with topical emollients in men with genital lichen sclerosus.	↑	
We **suggest** co-treatment with topical emollients in boys with genital lichen sclerosus.	↑	
We **suggest** co-treatment with topical emollients in patients with extragenital lichen sclerosus.	↑	

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SCUOLA DERMATOLOGICA SERGIO CHIMENTI

8.2.2 Topical and intralesional corticosteroids

Recommendation	Strength	Consensus
We **recommend** ultrapotent or potent topical corticosteroids in women with genital lichen sclerosus.	↑↑	>75% (16/17)[1] Evidence- and consensus-based
We **recommend** ultrapotent or potent topical corticosteroids in girls with genital lichen sclerosus.	↑↑	
We **recommend** ultrapotent or potent topical corticosteroids in men with genital lichen sclerosus.	↑↑	
We **recommend** ultrapotent or potent topical corticosteroids in boys with genital lichen sclerosus.	↑↑	
We **suggest** ultrapotent or potent topical corticosteroids in patients with extragenital lichen sclerosus.	↑	

[1]1 Abstention

Summary: no uniform recommendation possible:

- **Initial treatment:**
  - Clobetasol propionate 0.05% (ointment) or Mometasone furoate seem similarly effective.[219] Usually a fingertip unit is used.
  - Some recommend steroid ointments once daily for 3 months; others recommend 1 month daily, then slow reduction to e.g. alternate days application after daily Rx for another 2 months.

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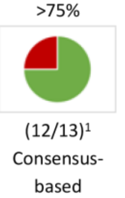
SCUOLA DERMATOLOGICA SERGIO CHIMENTI

We **recommend** the use of topical steroid ointments instead of creams or lotions in lichen sclerosus.	↑↑	>75%  (12/13)[1] Consensus-based

[1]1 Abstention

We **suggest** intralesional corticosteroids to hyperkeratotic lesions in women with topical steroid-resistant genital lichen sclerosus (provided malignancy has been excluded).	↑	>75% (15/16)[1] Evidence- and consensus-based
We **cannot make a recommendation** with respect to intralesional corticosteroids in girls with genital lichen sclerosus.	0	
We **cannot make a recommendation** with respect to intralesional corticosteroids in men with genital lichen sclerosus.	0	
We **cannot make a recommendation** with respect to intralesional corticosteroids in boys with genital lichen sclerosus.	0	
We **cannot make a recommendation** with respect to intralesional corticosteroids in patients with extragenital lichen sclerosus.	0	

triamcinolone acetonide or desametasone:

- in caso di mancate risposta

- scarso assorbimento per lesioni ipercheratosiche

8.2.3 Topical calcineurin inhibitors

Recommendation	Strength	Consensus
We **suggest** topical calcineurin inhibitors in women with genital lichen sclerosus as second choice or as an additional treatment if topical corticosteroids are contraindicated or insufficient. (off label)	↑	
We **suggest** topical calcineurin inhibitors in girls with genital lichen sclerosus as second choice or as an additional treatment if topical corticosteroids are contraindicated or insufficient. (off label)	↑	>75%
We **suggest** topical calcineurin inhibitors in men with genital lichen sclerosus as second choice or as an additional treatment if topical corticosteroids are contraindicated or insufficient. (off label)	↑	(15/16) Evidence- and consensus-based
We **suggest** topical calcineurin inhibitors in boys with genital lichen sclerosus as second choice or as an additional treatment if topical corticosteroids are contraindicated or insufficient. (off label)	↑	
We **cannot make a recommendation** with respect to topical calcineurin inhibitors in patients with extragenital lichen sclerosus. (off label)	0	

pimecrolimus 1% cream and tacrolimus 0.1% and 0.03%: 2vv/die fino a remissione, seguito da 1 vv al die pre 3- 6 mesi (off-label).

8.2.4 Topical retinoids

We **cannot make a recommendation** with respect to topical retinoids in women with genital lichen sclerosus. (off label)	0	100% 100 % Agreement (21/21) Evidence- and consensus-based
We **cannot make a recommendation** with respect to topical retinoids in girls with genital lichen sclerosus. (off label)	0	
We **cannot make a recommendation** with respect to topical retinoids in men with genital lichen sclerosus. (off label)	0	
We **cannot make a recommendation** with respect to topical retinoids in boys with genital lichen sclerosus. (off label)	0	
We **cannot make a recommendation** with respect to topical retinoids in patient with extragenital lichen sclerosus. (off label)	0	
Direct evidence available for: • Women: ○ 3 non-comparative/non-prospective studies (n=50) For specific results, see Evidence report		

Eritema e bruciore nel 35% delle pazienti

Donne in età fertile dovrebbero usare contraccezione

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8.2.5 Topical hormone preparations

Recommendation	Strength	Agreement
We **recommend against** topical testosterone and topical dihydrotestosterone in women as a treatment for genital lichen sclerosus.	↓↓	100% 100 % Agreement (16/16) Evidence- and consensus-based
We **recommend against** topical progesterone in women as a treatment for genital lichen sclerosus.	↓↓	
We **recommend against** topical oestrogen on the vulva in women as a treatment for genital lichen sclerosus. However, women may have additional genitourinary syndrome in which topical vaginal oestrogens may be helpful.	↓↓	
We **recommend against** topical hormone preparations in girls as a treatment for genital lichen sclerosus.	↓↓	
We **recommend against** topical hormone preparations in men as a treatment for genital lichen sclerosus.	↓↓	
We **recommend against** topical hormone preparations in boys as a treatment for genital lichen sclerosus.	↓↓	
We **recommend against** topical hormone preparations in in patients as a treatment for extragenital lichen sclerosus.	↓↓	

Direct evidence available for:

- Women:
  - Cochrane review (5 RCTs with testosterone, dihydrotestosterone, progesterone)
  - 1 RCT (testosterone)
    - Improvement of symptoms: GRADE ⊕◯◯◯ very low
  - 4 non-comparative/non-prospective (testosterone n=80); progesterone (n=60); clobetasol propionate + estradiol (n=17)

For specific results, see Evidence report

Nei pochi studi: efficacia inferiore ai css potenti o medio potenti

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8.3 Platelet rich plasma

We **cannot make a recommendation** with respect to platelet rich plasma in women with genital lichen sclerosus.	**0**	100% 100 % Agreement (21/21) Evidence- and consensus-based
We **cannot make a recommendation** with respect to platelet rich plasma in girls with genital lichen sclerosus.	**0**	
We **cannot make a recommendation** with respect to platelet rich plasma in men with genital lichen sclerosus.	**0**	
We **cannot make a recommendation** with respect to platelet rich plasma in boys with genital lichen sclerosus.	**0**	
We **cannot make a recommendation** with respect to platelet rich plasma in patients with extragenital lichen sclerosus.	**0**	

Direct evidence available for:

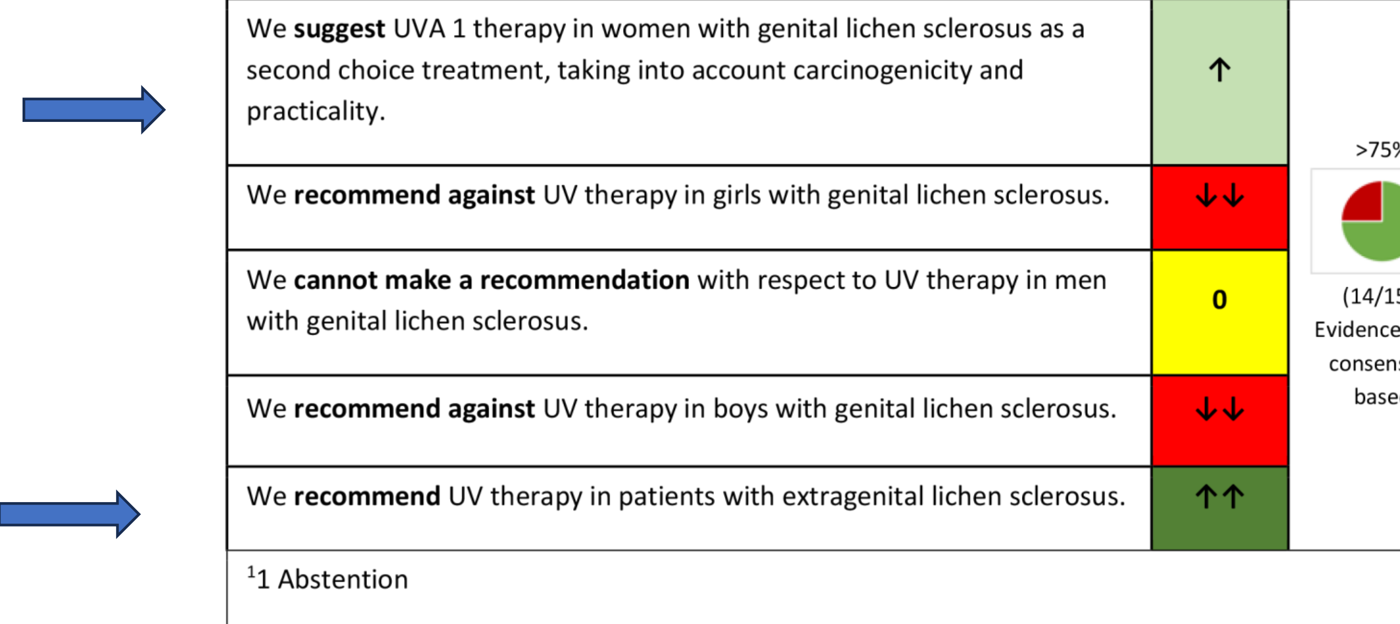
- Women:
    - 1 non-comparative/non-prospective study (n=28)
    - 1 non-comparative/non-prospective study (adipose-derived mesenchymal cells + platelet-rich plasma) (n=15)
- Females age unknown:
    - 1 non-comparative/non-prospective study (n=15)
    - 1 non-comparative/non-prospective study (adhesiolysis followed by PRP) (n=38)
- Men and boys:
    - 1 non-comparative/non-prospective study (n=45)
- Mixed adults:
    - 1 RCT (AD-SVF+PRP vs. AD-SVF) (n=40)
        - Improvement of symptoms: GRADE ⊕◯◯◯ very low
        - QoL: GRADE ⊕⊕◯◯ low
    - 1 non-comparative/non-prospective study (n=94)

For specific results, see Evidence report

In uno studio vs placebo non sono stati evidenti cambiamenti istologici e/o nell’infiltrato infiammatorio

Goldstein AT, Mitchell L, Govind V, Heller D. A randomized double-blind placebo-controlled trial of autologous platelet-rich plasma intradermal injections for the treatment of vulvar lichen sclerosus. *J Am Acad Dermatol*. Jun 2019;80(6):1788-1789.

8.4 UV therapy



Recommendation	Strength	Consensus
We **suggest** UVA 1 therapy in women with genital lichen sclerosus as a second choice treatment, taking into account carcinogenicity and practicality.	↑	>75% (14/15)[1] Evidence- and consensus based
We **recommend against** UV therapy in girls with genital lichen sclerosus.	↓↓	
We **cannot make a recommendation** with respect to UV therapy in men with genital lichen sclerosus.	0	
We **recommend against** UV therapy in boys with genital lichen sclerosus.	↓↓	
We **recommend** UV therapy in patients with extragenital lichen sclerosus.	↑↑	

[1] 1 Abstention

Basso dosaggio (20 J/cm²) or medio (50-50 J/cm²) UVA1 per 40 aaplicazioni per ciclo

La fototerapia UVA1 può essere associate alla terapia topica con css

UVA1 è piu' efficace dei NB-UV-B.

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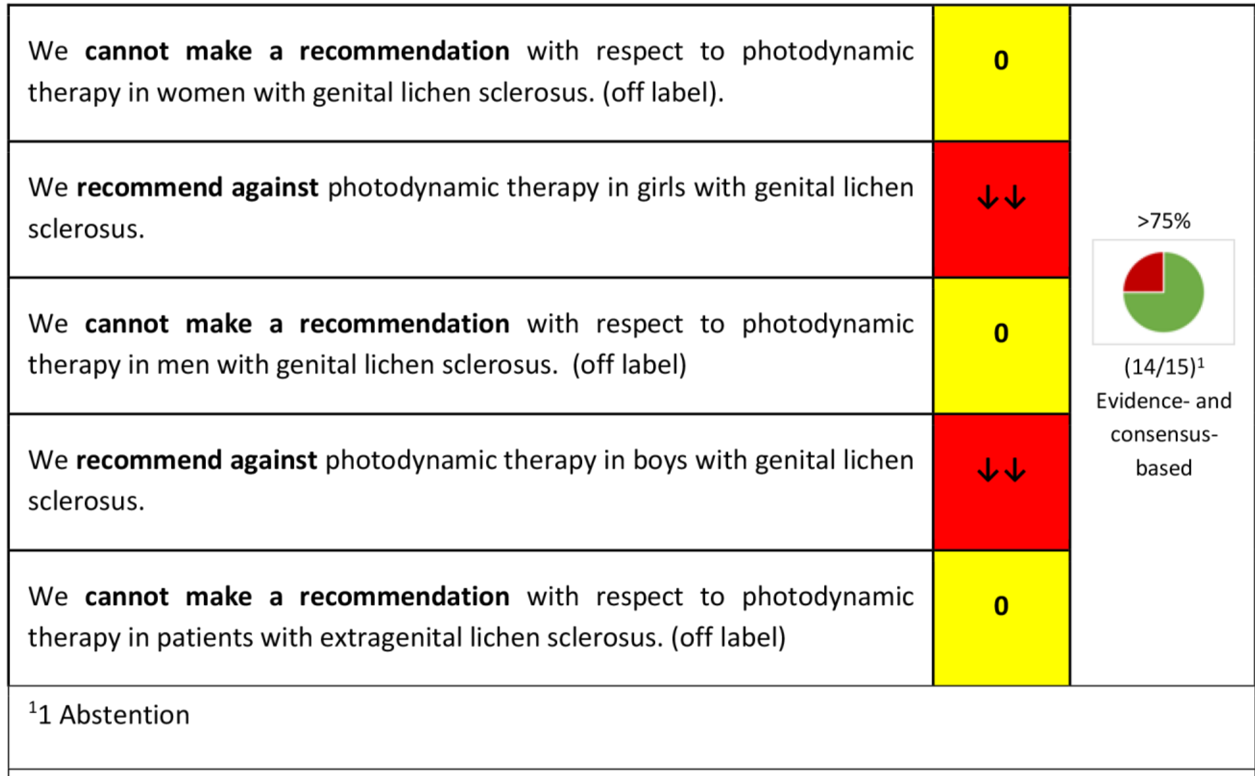
8.5 Photodynamic therapy



Recommendation	Strength	Consensus
We **cannot make a recommendation** with respect to photodynamic therapy in women with genital lichen sclerosus. (off label).	0	>75% (14/15)[1] Evidence- and consensus-based
We **recommend against** photodynamic therapy in girls with genital lichen sclerosus.	↓↓	
We **cannot make a recommendation** with respect to photodynamic therapy in men with genital lichen sclerosus. (off label)	0	
We **recommend against** photodynamic therapy in boys with genital lichen sclerosus.	↓↓	
We **cannot make a recommendation** with respect to photodynamic therapy in patients with extragenital lichen sclerosus. (off label)	0	

[1]1 Abstention

PDT is a valuable therapeutic option for vulval LS refractory to standard treatment with high potent topical corticosteroids.

PDT is particularly effective in terms of resolution of subjective symptoms, e.g. pruritus.

Doses might fluctuate between 9 and 180 J/cm2, with a range of 100–150 J/cm2
a minimum of 40 and a maximum of 700 mW/cm² can be applied. 3 to 5 PDT procedures might be necessary.

8.6 Laser therapy

Recommendation	Strength	Agreement
We **cannot make a recommendation** for fractionated ablative CO_2 laser treatment in women with genital lichen sclerosus.	0	100% 100 % Agreement (15/15) Evidence- and consensus-based
We **cannot make a recommendation** for non-ablative Nd:YAG laser in women with LS in order to soften the tissue.	0	
We **cannot make a recommendation** for ablative CO_2 laser treatment in men with genital lichen sclerosus.	0	
We **cannot make a recommendation** for non-ablative Nd:YAG laser in men with Lichen sclerosus in order to soften the tissue.	0	
We **cannot make a recommendation** with respect to laser treatment in patients with extragenital lichen sclerosus.	0	
We **cannot make a recommendation** for combination laser treatment in lichen sclerosus (e.g. ablative and non-ablative).	0	
We **recommend against using** laser treatment in children with Lichen sclerosus.	↓↓	

Direct evidence available for:

Fractionated CO2 : 10600 nm ablativo superficiale, riduce ipercheratosi ma non agisce sull'infiammazione

Nd:YAG : 1064 nm agisce nel derma ricude l'infiammazione e rimodella il collagene

Er:YAG : 2940 nm può essere utilizzato in moda ablativo e non ablativo

Dati non sempre coerenti, mancanza di gruppi controllo,, alcuni no modificazioni istologiche, o concomitante uso di css topici

NCT03665584: The purpose of this study is to look at the efficacy and safety of the **FxCO2 laser treatment** (laser energy emitted) for LS as compared to a sham treatment (very minimal laser energy emitted).
NCT05010421: In this prospective, randomized, open-label, comparative study, treatment success after 3 courses of **non-ablative treatment with CO2 laser** every 14 days will be compared with treatment success after topical application of clobetasol 0.05% over 3 months (daily in the first month, every other day in month 2, and 3 times/week during month 3) at the time point 3 months after treatment initiation.

NCT03926299: The aim of this study is to test a new, minimally invasive dual laser technique to treat vulval LS. Efficacy and safety of the thermal **non-ablative Nd:YAG laser** and the **ablative Er:YAG laser** (FotonaSmooth SP® Spectro laser device) is determined and compared to the current standard treatment with high dose topical steroids. The hypothesis is that laser therapy is effective and similar to standard steroid therapy. Results are expected in 2023.

8.7 Cryotherapy

We **cannot make a recommendation** with respect to cryotherapy in women with genital lichen sclerosus.	0	100% 100 % Agreement (21/21) Evidence- and consensus-based
We **cannot make a recommendation** with respect to cryotherapy in girls with genital lichen sclerosus.	0	
We **cannot make a recommendation** with respect to cryotherapy in men with genital lichen sclerosus.	0	
We **cannot make a recommendation** with respect to cryotherapy in boys with genital lichen sclerosus.	0	
We **cannot make a recommendation** with respect to cryotherapy in patients with extragenital lichen sclerosus.	0	
Direct evidence available for: • Women and girls: ○ 1 non-comparative/non-prospective study (n=31) For specific results, see Evidence report		

Uno studio retrospettivo 22 adulti e 9 adolescent con LS vulvare ha mostrato miglioramento soprattutto del prurito.

Kastner U, Altmeyer P. [Cryosurgery--the last resort or a surgical alternative in the treatment of lichen sclerosus et atrophicus of the vulva (LSAV)?]. J Dtsch Dermatol Ges. Mar 2003;1(3):206-11. Kryochirurgie--ultima ratio oder chirurgische Alternative beim vulvären Lichen sclerosus et atrophicus (LSAV)?

8.8 Systemic treatment

Recommendation	Strength	Consensus
We **suggest** acitretin, taking into account teratogenicity, if systemic therapy is needed in women with genital lichen sclerosus. (off label)	↑	>75% (17/18)[1] Evidence- and consensus-based
We **suggest** acitretin if systemic therapy is needed in men with genital lichen sclerosus,. (off label)	↑	>75% (15/17)[2] Evidence- and consensus-based
We **suggest** MTX, taking into account teratogenicity, if systemic treatment is needed in adult patients with genital and/or extragenital lichen sclerosus,. (off label)	↑	>75% (15/16)[1] Consensus-based
We **recommend against** potassium para-aminobenzoate as a treatment for lichen sclerosus.	↓↓	100% 100 % Agreement (15/15) Evidence- and consensus-based

[1]1 Abstention

[2]2 Abstention

TERAPIA SISTEMICA in caso di LS con manifestazioni extragenitali: prima scelta MTX e acitretina (off-label)

Paramino-benzoato di potassio: differenze non statisticamente significative

Buxton P, Priestley G. Para-aminobenzoate in lichen sclerosus et atrophicus. Journal of Dermatological Treatment. 1990;1(5):255-256.

Doxiciclina può essere considerata come tp anche se non ci sono studi ma sono serie di case report.

Shelley WB, Shelley ED, Amurao CV. Treatment of lichen sclerosus with antibiotics. Int J Dermatol. Sep 2006;45(9):1104-6.

Casi sporadici di successo con: dupilumab, secukinumab e adalimumab

Peterson DM,et al . Treatment of lichen sclerosus and hypertrophic scars with dupilumab. JAAD Case Rep. May 2022;23:76-78.

Ye Q,et al. Generalized lichen sclerosus et atrophicus combined with ankylosing spondylitis responding to secukinumab. Scand J Rheumatol. Sep 20 2022:1-2.

Lowenstein EB, Zeichner JA. Intralesional adalimumab for the treatment of refractory balanitis xerotica obliterans. JAMA Dermatol. Jan 2013;149(1):23-4.

Terapia sistemica: retinoidi

- Miglioramento dei sintomi in 6 su 8 pt con etretinato 1mg/kg/day

Mørk NJ, Jensen P, Hoel PS. Vulval lichen sclerosus et atrophicus treated with etretinate (Tigason). Acta Derm Venereol. 1986;66(4):363-5.)

- Miglioramento dei sintomi Etretinato 0,54mg/kg/day con successivo mantenimento a 0,26 mg/kg/day

(Romppanen U, Tuimala R, Ellmén J, Lauslahti K. Oral treatment of vulvar dystrophy with an aromatic retinoid, etretinate]. Geburtshilfe Frauenheilkd. Apr 1986;46(4):242-7).

- In uno studio multicentrico doppio cieco con 20-30 mg di acitretina vs placebo per 16 sett. Si è osservato un miglioramento del prurito atrofia e ipercheratosi.

Bousema MT, et al. Acitretin in the treatment of severe lichen sclerosus et atrophicus of the vulva: a double-blind, placebo-controlled study. J Am Acad Dermatol. Feb 1994;30(2 Pt 1):225-31.

Terapia sistemica: methotrexate

- Uno studio retrospettivo su 28 pts con coinvolgimento extracutaneo trattati con MTX 2,5 a 17,5 mg a sett. Un miglioramento parziale in 21/28 e 15/28 miglioramento importante.

Cuellar-Barboza A, et al. Methotrexate for the treatment of recalcitrant genital and extragenital lichen sclerosus: A retrospective series. Dermatol Ther. Jul 2020;33(4)

- Studio su 7 pts con LS con coinvolgimento extracutaneo (5 genitale+ cute, 2 solo cute) trattati metilprednisolone in bolo per 3 gg e successivamente con MTX 15mg a sett. Miglioramento cutaneo riportato ma non è riportato esito genitale

Kreuter A,et al. Pulsed high-dose corticosteroids combined with low-dose methotrexate treatment in patients with refractory generalized extragenital lichen sclerosus. Arch Dermatol. Nov 2009;145(11):1303-8. 352. Nayeemuddin F, Yates VM. Lichen sclerosus et atrophicus responding to methotrexate. Clin Exp Dermatol. Aug 2008;33(5):651-2.

- Un paziente con LS genitale e cutaneo trattato con MTX 10mg/sett per 2 mesi con successo e mantenimento fino a 5 mesi.

Nayeemuddin F, Yates VM. Lichen sclerosus et atrophicus responding to methotrexate. Clin Exp Dermatol. Aug 2008;33(5):651-2.

10. Lichen sclerosus in pregnancy

In most women, lichen sclerosus does not worsen during pregnancy and may even improve.	**Statement**	>75% (14/16)[1] Expert Consensus

[1]1 Abstention

We **recommend** vaginal delivery in women with lichen sclerosus, unless there are contraindications.	↑↑	>75% (9/10) Consensus-based

Lichen sclerosus seems not to be associated with impaired post-procedure perineal wound healing.	**Statement**	>75% (14/15)[1] Expert Consensus

[1]1 Abstention

We **recommend** maintenance treatment during pregnancy, consisting of a potent TCS, such as mometasone furoate, with the minimum frequency needed to control the disease.	↑↑	>75% (14/15)[1] Expert Consensus

[1]1 Abstention

We **cannot make a recommendation** with regard to the use of topical corticosteroid injection (TCI) during pregnancy and breastfeeding in lichen sclerosus patients.	**0**	>50% (12/16)[1] Expert Consensus

[1]2 Abstention

Durante la gravidanza: non si assista ad un peggioramento clinico o dei sintomi, inoltre non sembra che vi sia associazione con complicanze legate a parto e/o alla cicatrizzazione.

La scelta di prima linea sono I css topici potenti o ultrapotenti
Studi hanno dimostrato la sicurezza per piccole area da trattare.

Lee A, Bradford J, Fischer G. Long-term Management of Adult Vulvar Lichen Sclerosus: A Prospective Cohort Study of 507 Women. JAMA Dermatol.

Gli inibirtori della calcineurina non sono indicate in gravidanza e allattamento.

Dermatology Update
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conclusioni

G Kirtschig[1], M Kinberger[2], A Kreuter[3], R Simpson[4], A Günthert[5], C van Hees[6], K Becker[7], MJ Ramakers[8], M Corazza[9], S Müller[10], S von Seitzberg[11], MJ Boffa[12], R Stein[13], G Barbagli[14], CC Chi[15,16], JN Dauendorffer[17], B Fischer[18], M Gaskins[2], E Hiltunen-Back[19], A Höfinger[18], NH Köllmann[18], H Kühn[20], HK Larsen[21] M Lazzeri[22], W Mendling[23], AF Nikkels[24], M Promm[25], KK Rall[26], S Regauer[27], M Sárdy[28], N Sepp[29], T Thune[30], A Tsiogka[31], S Vassileva[32], L Voswinkel[23], L Wölber[33], RN Werner[2]

Terapia di prima linea:

- css topico ultrapotenti o potenti

Terapia di seconda linea:

- inibitori topici della calcineurina (off-label)
- Css intralesionali, in caso ipercheratosi
- fototerapia nelle forme extragenitali o genitali nelle donne
- Terapia sistemica con retinoidi, methotrexate o doxiciclina