



La patologia infiammatoria genitale

Alessandro Borghi

Dipartimento di Scienze Mediche, Sezione di Dermatologia e Malattie Infettive

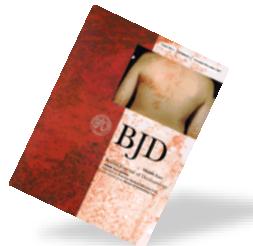
Università degli Studi di Ferrara

Direttore: Prof. Monica Corazza

lichen sclerosus: prima scelta

2012

□ clobetasolo propionato (CP) 0.05% unguento / crema



BJD © 2010 British Association of Dermatologists 2010 163, pp672–682

British Association of Dermatologists' guidelines for the management of lichen sclerosus 2010

S.M. Neill, F.M. Lewis,* F.M. Tatnall† and N.H. Cox‡

the recommended and accepted first-line treatment is the very potent topical corticosteroid clobetasol propionate 0.05%^{56–58} (Strength of recommendation B; quality of evidence 2++; see Appendix for definitions).

J Am Acad Dermatol 2012;67:305-12.

FROM THE COCHRANE LIBRARY

Systematic review and meta-analysis of randomized controlled trials on topical interventions for genital lichen sclerosus

Ching-Chi Chi, MD, MMS, DPhil,^a Gudula Kirtschig, MD, PhD,^b Maha Baldo, MD,^c Fiona Lewis, MD,^{d,c} Shu-Hui Wang, MD, MS,^f and Fenella Wojnarowska, DM^e

The very potent topical steroid, clobetasol propionate 0.05%, was found to be significantly more effective than placebo in treating genital lichen sclerosus



corticosteroidi alternativi

metilprednisolone furoato 0.1% crema

Cattaneo A et al. Topical mometasone furoate for vulvar lichen sclerosus. *J Reprod Med* 2003; 48: 444-8.

triamcinolone acetonide 0.1% unguento

LeFevre C et al. Management of lichen sclerosus with triamcinolone ointment: effectiveness in reduction of patient symptom scores. *J Low Genit Tract Dis* 2011; 15:205-9.

metilprednisolone aceponato 0.1% crema

Patsatsi A et al. A therapeutic approach for female, relapsing genital lichen sclerosus: a single-center study. *J Dermatolog Treat* 2013; 24: 336-9.

idrocortisone 0.1% unguento, betametasone dipropionato 0.05% unguento

Bradford J et al. Long-term management of vulval lichen sclerosus in adult women. *Aust N Z J Obstet Gynaecol* 2010 ; 50:148-52.



corticosteroidi alternativi



ORIGINAL ARTICLE

JEADV 2014, 28, 943–948

Mometasone fuoroate 0.1% ointment in the treatment of vulvar lichen sclerosus: a study of efficacy and safety on a large cohort of patients

A. Virgili,* A. Borghi, S. Minghetti, M. Corazza

MMF 0.1% unguento in trattamento di fase acuta 12 settimane

- 5/settimana per 4 settimane
- a dì alterni per 4 settimane
- 2/settimana per 4 settimane

147 pazienti affette da VLS

- 113 pazienti (80.7%) responsive (*responder*)
- ↓ significativa dei sintomi, anche nelle *non responder*
- buona tollerabilità

...ma



J Am Acad Dermatol 2012;67:305-12.

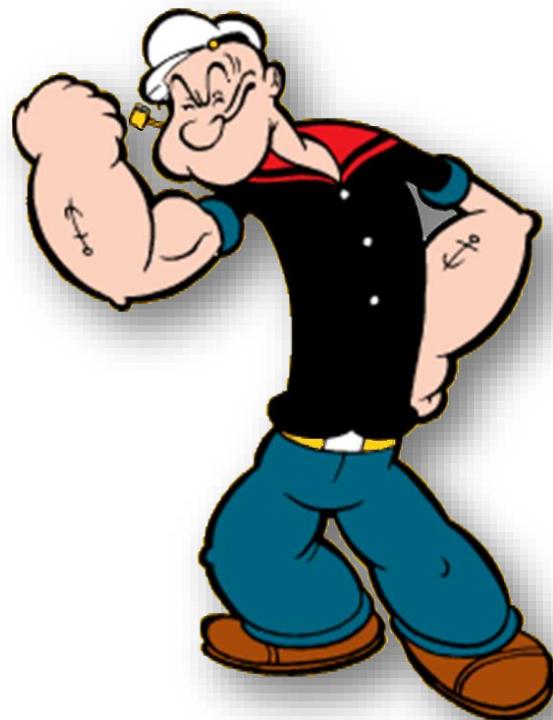
FROM THE COCHRANE LIBRARY

Systematic review and meta-analysis of randomized controlled trials on topical interventions for genital lichen sclerosus

Ching-Chi Chi, MD, MMS, DPhil,^a Gudula Kirtschig, MD, PhD,^b Maha Baldo, MD,^c Fiona Lewis, MD,^{d,e} Shu-Hui Wang, MD, MS,^f and Fenella Wojnarowska, DM^c

Implications for research. The current evidence is limited, and further studies are required to fill in gaps in knowledge. First, we need RCTs determining the potency and regimen (eg, frequency and duration of application) of topical corticosteroids that have adequate therapeutic efficacy but with the least desirable adverse effects (eg, infections and atrophy)

potenza





RCT: CP vs MMF

British Journal of Dermatology (2014) 171, pp388–396

First randomized trial on clobetasol propionate and mometasone furoate in the treatment of vulvar lichen sclerosus: results of efficacy and tolerability

A. Virgili, A. Borghi, G. Toni, S. Minghetti and M. Corazza

Class I *superpotent*
CLOBETASOL PROPIONATE 0.05%

Class II *potent*
MOMETASONE FUROATE oint 0.1%

Class III *mild*
FLUOCINOLONE ACETONIDE cr 0.025%

Class IV *least potent*
HYDROCORTISONE 0.5%

clobetasolo propionato 0.05% unguento

VS

mometasone furoato 0.1% unguento

in trattamento di fase acuta 12 settimane

- 5/settimana per 4 settimane
- a dì alterni per 4 settimane
- 2/settimana per 4 settimane

Class I *superpotent*
CLOBETASOL PROPIONATE 0.05%

Class II *potent*
MOMETASONE FUROATE oint 0.1%

Class III *potent*
BETAMETHASONE VALERATE oint 0.1%

Class IV *midstrength*
MOMETASONE FUROATE cr 0.1%

Class V *midstrength*
FLUOCINOLONE ACETONIDE cr 0.025%

Class VI *mild*
TRIAMCINOLONE AC oint 0.1%

Class VII *least potent*
HYDROCORTISONE 0.5%



RCT: CP vs MMF

British Journal of Dermatology (2014) 171, pp388–396

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clobetasolo propionato 0.05% unguento

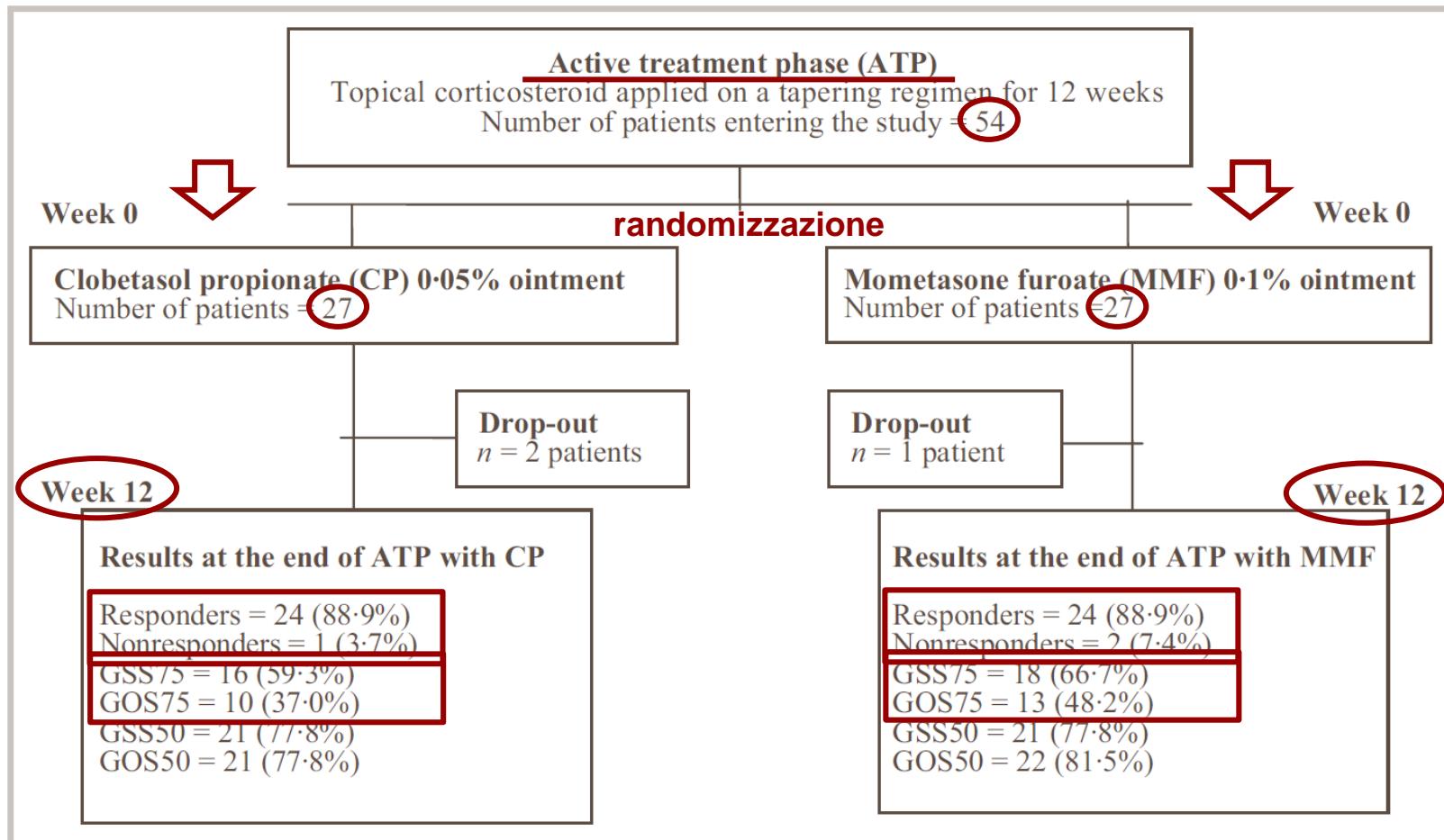
VS

mometasone furoato 0.1% unguento

- ⇨ **efficacia**
- ⇨ **sicurezza**
- ⇨ **aderenza e soddisfazione**



risultati



British Journal of Dermatology (2014) 171, pp388–396

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risultati

tollerabilità del trattamento:

non effetti collaterali legati alla terapia



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In conclusion, these results provide evidence that MMF is as effective as CP in the treatment of VLS; consistent with this, MMF could represent an effective alternative to CP as a firstline treatment for the disease.

posologia



posologia



BJD © 2010 British Association of Dermatologists 2010 **163**, pp672–682

**British Association of Dermatologists' guidelines for the
management of lichen sclerosus 2010**

S.M. Neill, F.M. Lewis,* F.M. Tatnall† and N.H. Cox‡

There are no randomized controlled trials providing evidence that a once- or twice-daily application of any one specific corticosteroid is the most effective, or documenting that one regimen is superior to another.





RCT: continuo vs *tapering*

British Journal of Dermatology (2015) 173, pp1381–1386

CLINICAL TRIALS

British Journal of Dermatology

Continuous vs. tapering application of the potent topical corticosteroid mometasone furoate in the treatment of vulvar lichen sclerosus: results of a randomized trial

A. Borghi, M. Corazza, S. Minghetti, G. Toni and A. Virgili

mometasone furoato 0.1% ung vs mometasone furoato 0.1% ung

in trattamento di fase acuta 12 settimane

continuativo

vs

tapering

5/settimana per 12 settimane

5/settimana per 4 settimane

a dì alterni per 4 settimane

2/settimana per 4 settimane



RCT: continuo vs *tapering*

British Journal of Dermatology (2015) 173, pp1381–1386

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mometasone furoato 0.1% ung vs mometasone furoato 0.1% ung

continuativo

- 5/settimana per 12 settimane

⇨ **efficacia**

⇨ **sicurezza**

⇨ **aderenza**

vs

tapering

- 5/settimana per 4 settimane
- a dì alterni per 4 settimane
- 2/settimana per 4 settimane



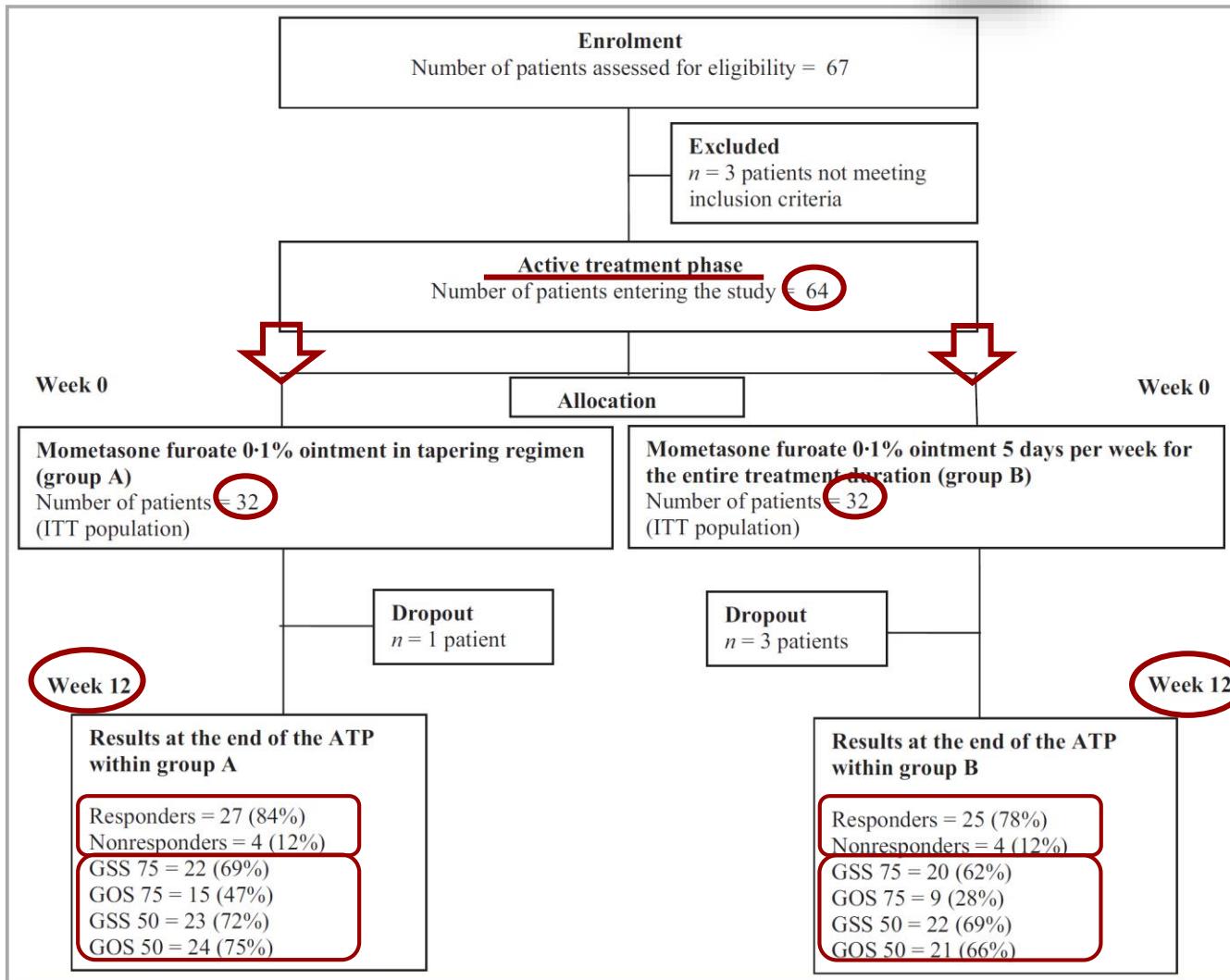
risultati



CLINICAL TRIALS

British Journal of Dermatology (2015) 173, pp1381–1386

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CLINICAL TRIALS

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tollerabilità del trattamento:

non effetti collaterali legati alla terapia



risultati



British Journal of Dermatology (2015) 173, pp1381–1386

British Journal of Dermatology

BJD

CLINICAL TRIALS
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A. Borghi, M. Corazza, S. Minghetti, G. Toni and A. Virgili

□ aderenza al trattamento:

mometasone furoato 0.1% ung vs mometasone furoato 0.1% ung



continuativo

tapering

relative risk: **2.14** (95% confidence interval 0.20–22.34)
 $p = 0.60$





RCT: continuo vs tapering

British Journal of Dermatology (2015) 173, pp1381–1386

CLINICAL TRIALS

BJD

British Journal of Dermatology

Continuous vs. tapering application of the potent topical corticosteroid mometasone furoate in the treatment of vulvar lichen sclerosus: results of a randomized trial

A. Borghi, M. Corazza, S. Minghetti, G. Toni and A. Virgili

Our findings seem to indicate strongly that both tapering and continuous application of MMF have similar efficacy and tolerability in treating active VLS, with both well tolerated and effective in improving the symptoms and signs of the disease. No significant differences in patient adherence to the two study protocols were found.

In conclusion, these results confirm the usefulness of topical potent corticosteroids in the ATP of VLS, and provide evidence that they can be administered equally well in a continuous or tapering regimen.

formulazione



JOURNAL OF DERMATOLOGICAL TREATMENT, 2017

Mometasone furoate in the treatment of vulvar lichen sclerosus: could its formulation influence efficacy, tolerability and adherence to treatment?

Monica Corazza, Annarosa Virgili, Giulia Toni and Alessandro Borghi

mometasone furoato 0.1% **crema** vs mometasone furoato 0.1% **unguento**

	Patients treated with MMF cream (group A)	Patients treated with MMF ointment (group B)	p
Responders, n (%)	16 (59.26)	29 (78.38)	.09
GSS75, n (%)	12 (44.44)	25 (67.57)	.06
GOS75, n (%)	11 (40.74)	17 (45.95)	.67
GSS50, n (%)	21 (77.78)	30 (81.08)	.74
GOS50, n (%)	19 (70.37)	30 (81.08)	.31

formulazione



JOURNAL OF DERMATOLOGICAL TREATMENT, 2017

Mometasone furoate in the treatment of vulvar lichen sclerosus: could its formulation influence efficacy, tolerability and adherence to treatment?

Monica Corazza, Annarosa Virgili, Giulia Toni and Alessandro Borghi

Our findings indicate that MMF in ointment formulation is more effective in treating active VLS, especially in improving symptoms, in comparison with MMF cream. Both formulations were well tolerated and no significant differences in patient adherence and satisfaction with the treatment were found.

In conclusion, based on these results the ointment vehicle seems to optimize the therapeutic action of potent corticosteroids and thus could be preferable to the cream for the treatment of VLS.

...ma



J Am Acad Dermatol 2012;67:305-12.

FROM THE COCHRANE LIBRARY

Systematic review and meta-analysis of randomized controlled trials on topical interventions for genital lichen sclerosus

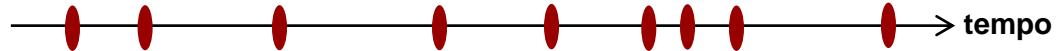
Ching-Chi Chi, MD, MMS, DPhil,^a Gudula Kirtschig, MD, PhD,^b Maha Baldo, MD,^c Fiona Lewis, MD,^{d,e} Shu-Hui Wang, MD, MS,^f and Fenella Wojnarowska, DM^c

Implications for research. ...one of our secondary outcomes, “duration of remission or prevention of subsequent flares,” should be included in future RCTs

mantenimento

...a lungo termine?

1. terapia reattiva



BJD © 2010 British Association of Dermatologists 2010 **163**, pp672–682

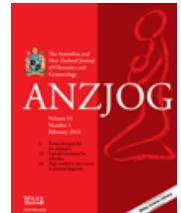
British Association of Dermatologists' guidelines for the management of lichen sclerosus 2010

S.M. Neill, F.M. Lewis,* F.M. Tatnall† and N.H. Cox‡

About 60% of patients experience complete remission of their symptoms.^{60,61}
Others will continue to have flares and remissions; they are advised to use
clobetasol propionate 0.05% **as required.**

...a lungo termine?

1. terapia reattiva
2. terapia protratta

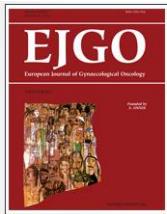


Australian and New Zealand Journal of Obstetrics and Gynaecology 2010; 50: 148–152

Long-term management of vulval lichen sclerosus in adult women

J. BRADFORD¹ and G. FISCHER²

- metilprednisolone aceponato 0.1% crema
 - idrocortisone 0.1% unguento
 - betametasone dipropionato 0.05% unguento
- } 12 mesi



Eur J Gynaecol Oncol. 2002; 23: 519-22.

**Vulvar lichen sclerosus in postmenopausal women:
a comparative study for treating advanced disease
with clobetasol propionate 0.05%.**

Diakomanolis ES¹, Haidopoulos D, Syndos M, Rodolakis A, Stefanidis K, Chatzipapas J, Michalas S.

clobetasolo propionato per 6 mesi vs al bisogno



JAMA Dermatology Published online June 12, 2015

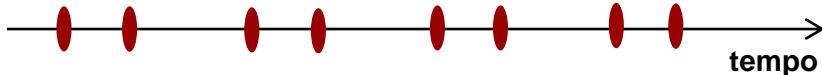
**Long-term Management of Adult Vulvar Lichen Sclerosus
A Prospective Cohort Study of 507 Women**

Andrew Lee, MBBS; Jennifer Bradford, MBBS; Gayle Fischer, MD

corticosteroide OO

...a lungo termine?

1. terapia reattiva
2. terapia protratta
3. **terapia proattiva**



British Journal of Dermatology (2013) 168, pp1316–1324

**Proactive maintenance therapy with a topical corticosteroid
for vulvar lichen sclerosus: preliminary results of a
randomized study**

A. Virgili, S. Minghetti, A. Borghi and M. Corazza

MMF 0.01% unguento, **2 applicazioni /settimana** per 12 mesi

RCT: MMF proattiva

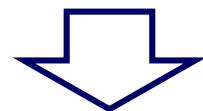


British Journal of Dermatology (2013) 168, pp1316–1324

**Proactive maintenance therapy with a topical corticosteroid
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randomized study**

A. Virgili, S. Minghetti, A. Borghi and M. Corazza

mometasone furoato 0.1% ung per 12 settimane (ATP)



rispondere

RCT: MMF proattiva



British Journal of Dermatology (2013) 168, pp1316–1324

**Proactive maintenance therapy with a topical corticosteroid
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responder



12 mesi

MMF 0.01% unguento, 2 applicazioni /settimana

vs

crema base, 1 applicazione / die

vs

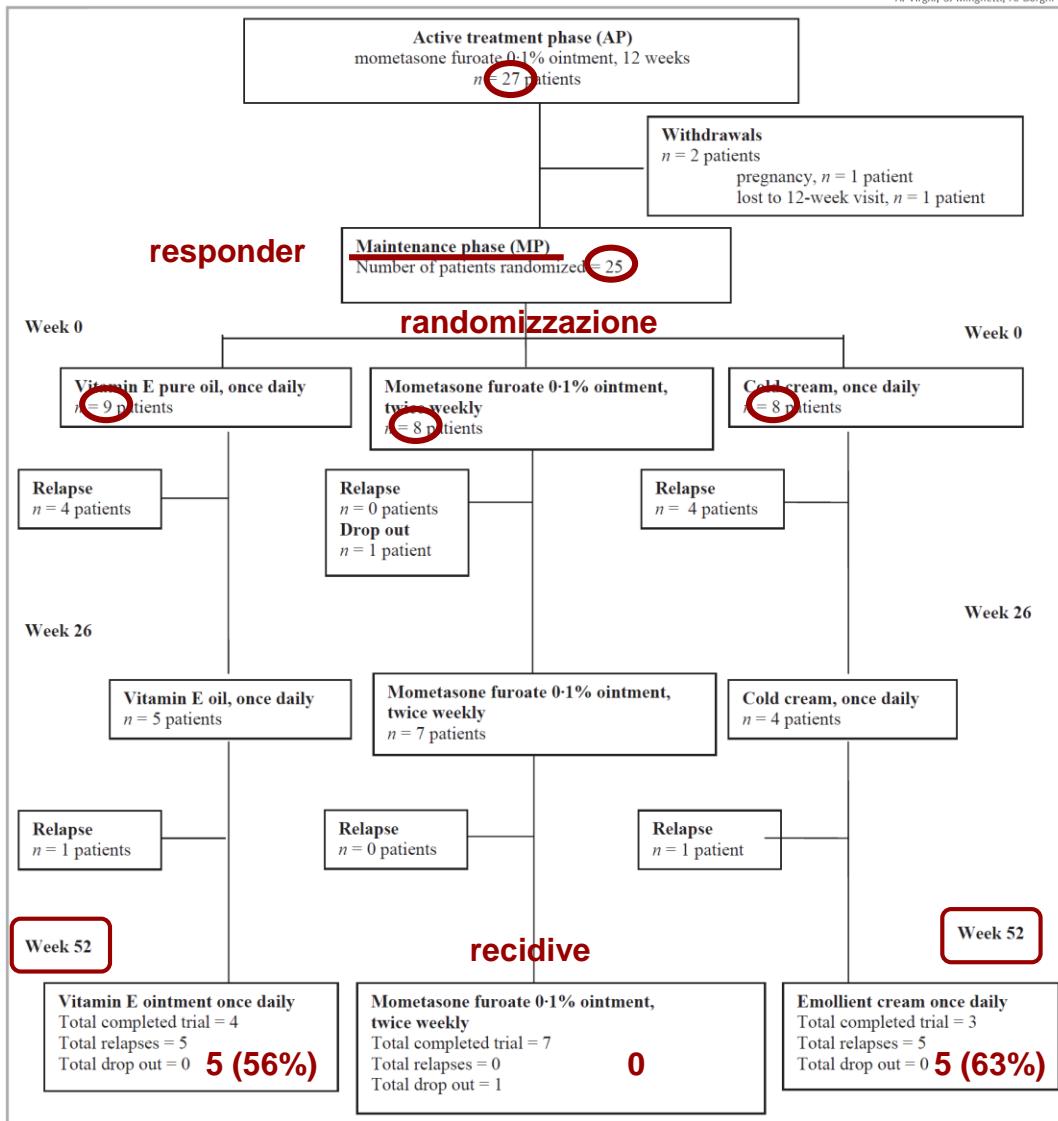
vitamina E, 1 applicazione / die

risultati

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risultati

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MMF 0.01% unguento, 2 applicazioni /settimana

vs

crema base, 1 applicazione / die $p = 0.0128$

vs

vitamina E, 1 applicazione / die $p = 0.0204$

recidiva

RR = 0.0951 (95% CI 00177– 05106)



RCT: MMF proattiva



British Journal of Dermatology (2013) 168, pp1316–1324

Proactive maintenance therapy with a topical corticosteroid for vulvar lichen sclerosus: preliminary results of a randomized study

A. Virgili, S. Minghetti, A. Borghi and M. Corazza

In conclusion, these results provide evidence that maintenance treatment with mometasone furoate 0.1% ointment twice weekly may play an important role in clinical practice and could represent the treatment of choice in the challenging long-term management of VLS.

RCT: MMF vs CP proattiva



British Journal of Dermatology (2014) 171, pp388–396

First randomized trial on clobetasol propionate and mometasone furoate in the treatment of vulvar lichen sclerosus: results of efficacy and tolerability

A. Virgili, A. Borghi, G. Toni, S. Minghetti and M. Corazza

Clobetasol propionate vs. mometasone furoate in 1-year proactive maintenance therapy of vulvar lichen sclerosus: results from a comparative trial

M. Corazza, A. Borghi,* S. Minghetti, G. Toni, A. Virgili

CP 0.05% unguento vs MMF 0.1% unguento



responder



responder

mantenimento

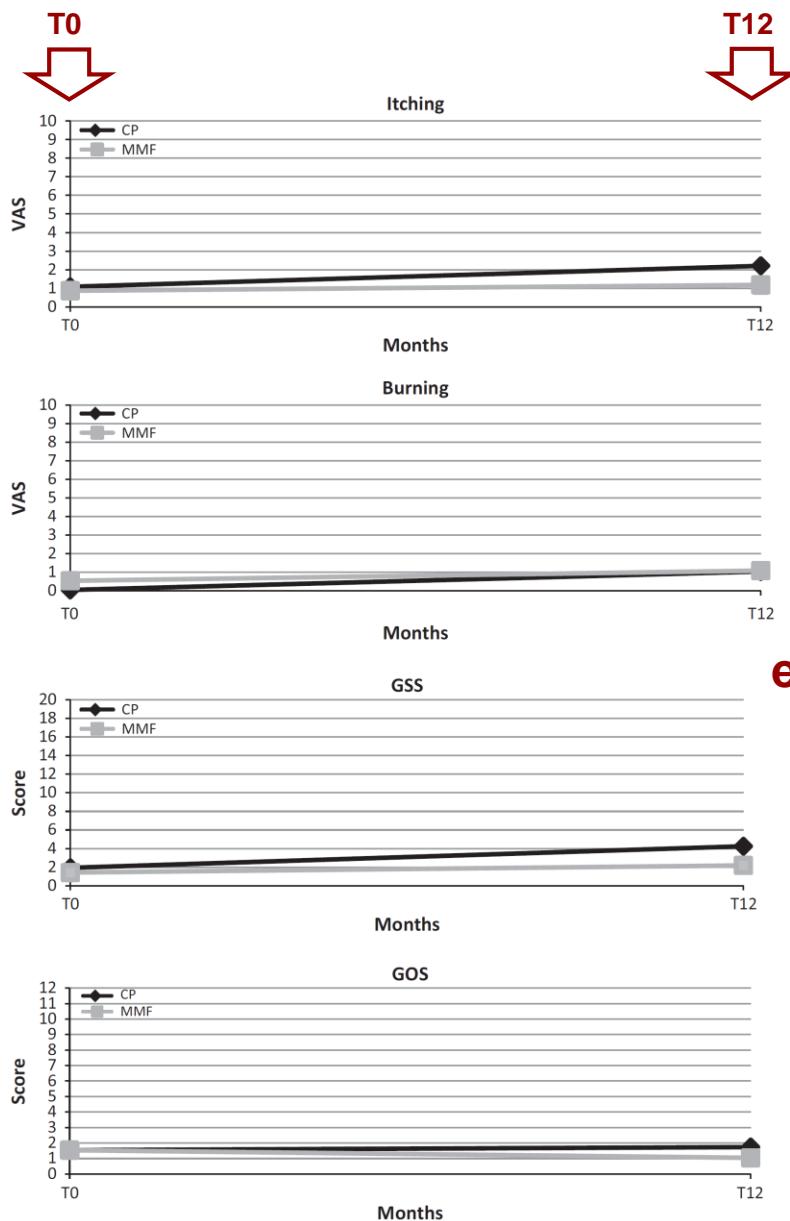
12 mesi

CP 0.05% unguento vs MMF 0.1% unguento

2 applicazioni / settimana



risultati



Clobetasol propionate vs. mometasone furoate in 1-year proactive maintenance therapy of vulvar lichen sclerosus: results from a comparative trial

M. Corazza, A. Borghi,* S. Minghetti, G. Toni, A. Virgili

p = ns

tra T0 e T12

efficacia della proattiva nel mantenimento

CP vs MMF

non differenze tra corticosteroidi

RCT: MMF vs CP proattiva



Clobetasol propionate vs. mometasone furoate in 1-year proactive maintenance therapy of vulvar lichen sclerosus: results from a comparative trial

M. Corazza, A. Borghi,* S. Minghetti, G. Toni, A. Virgili

The study results provide evidence that proactive treatment with either CP 0.05% ointment or MMF 0.1% ointment is an effective, safe and reliable therapy for the long-term prevention of relapse in VLS previously treated with topical corticosteroid.

clearance

Cure is not usually the aim of treatment but improvement of symptoms (75–95%) after 3 months or at its best reversals of signs (20%) (1+/A).

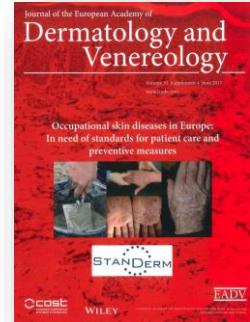


JEADV 2015, 29, e1–e43

GUIDELINES

Evidence-based (S3) Guideline on (anogenital) Lichen sclerosus

G. Kirtschig,^{1,2,*} K. Becker,³ A. Günthert,⁴ D. Jasaitiene,⁵ S. Cooper,⁶ C.-C. Chi,^{7,8} A. Kreuter,⁹ K.K. Rall,¹⁰ W. Aberer,¹¹ S. Riechardt,¹² F. Casabona,¹³ J. Powell,¹⁴ F. Brackenbury,¹⁵ R. Erdmann,¹⁶ M. Lazzeri,¹⁷ G. Barbagli,¹⁷ F. Wojnarowska¹⁸



clearance

JEADV 2018, 32, 96–101

Clearance in vulvar lichen sclerosus: a realistic treatment endpoint or a chimera?

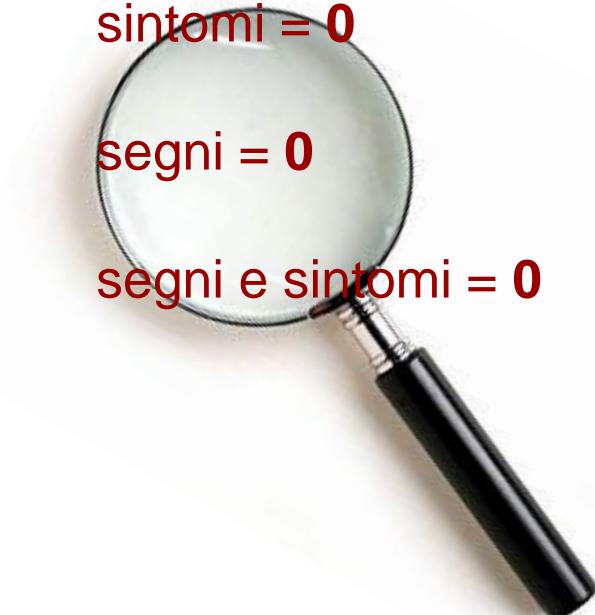
A. Borghi,* A. Virgili, S. Minghetti, G. Toni, M. Corazza

studio retrospettivo su **196 pazienti trattate per 12 settimane**

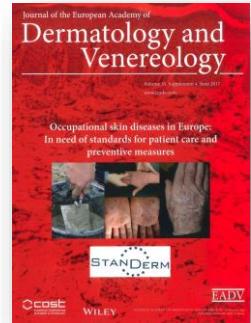
sintomi = 0

segni = 0

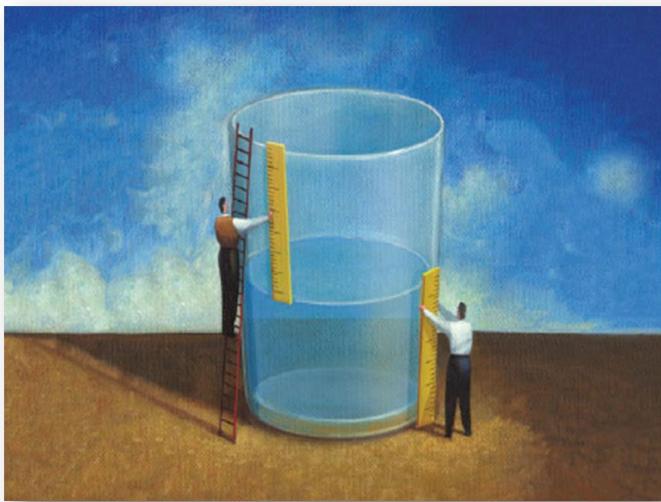
segni e sintomi = 0



Patients (n.)	Treatment regimen (12-week duration)
79	0.1% of MMF ointment once daily, at tapering regimen, as previously described ^{1,2}
52	0.1% of MMF ointment once daily for five consecutive days per week
27	0.05% of CP ointment once daily, at tapering regimen, as previously described ^{1,2}
21	0.1% of MMF ointment and 0.05% of tretinoin cream, for five consecutive days per week
17	0.025% of tretinoin cream once daily, every other day



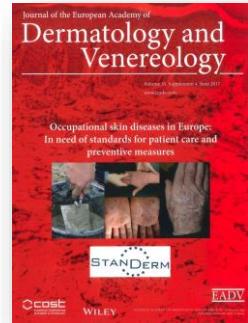
clearance



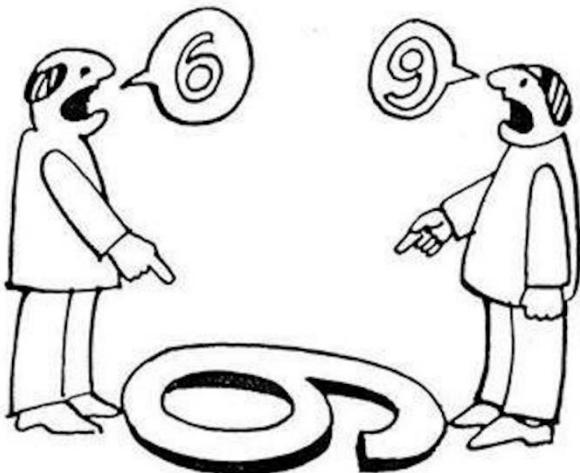
Clearance in vulvar lichen sclerosus: a realistic treatment endpoint or a chimera?

A. Borghi,* A. Virgili, S. Minghetti, G. Toni, M. Corazza

- (i) 165 pz sintomatiche al *baseline* → **GSS = 0** in 78 pz (**47.3%**)
- (ii) 187 pz che hanno completato la terapia → **GOS = 0** in 40 pz (**21.4%**)
- (iii) 165 pz sintomatiche al *baseline* → **complete clearance** in 23 pz (**13.9%**)
- (iv) 59 pazienti con **dispareunia** → 18 pz (**30.5%**) risoluzione del sintomo



clearance



Clearance in vulvar lichen sclerosus: a realistic treatment endpoint or a chimera?

A. Borghi,* A. Virgili, S. Minghetti, G. Toni, M. Corazza

In conclusion, a 12-week topical treatment, although highly effective in ameliorating both symptoms and objective changes, is unlikely to induce a complete cure of VLS. As a result, a relevant part of the patients labelled as responders are not actually clear of the disease, and this may account for a divergence between physicians' and patients' perspectives regarding treatment outcome and satisfaction.

memoranda

- corticosteroidi **potenti** e **ultra-potenti** pari efficacia e tollerabilità nella terapia di attacco  **prima linea terapeutica**
- posologia **continuativa** e **tapering** pari efficacia e tollerabilità nella terapia di attacco
- **unguento maggiore efficacia** di crema
- terapia **corticosteroidea proattiva** efficace e sicura nel **mantenimento** a lungo termine

memoranda

- ***clearance obiettivo difficile*** da raggiungere in 12 settimane

