

Supplementary files

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Disorders with Level 1 evidence and lower

Atopic dermatitis <2 years of age

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs				
Lee et al. (2014)	R, DB, C trial (28)	+	1326	P ~ TCS (infants 3-23 mts)
Papp et al. (2004)	R, DB, VC (250)	+		P (analysis by age; 3-23 mts group)
Kapp et al. (2002)	R DB, C trial (204)	+		P (3-23 mts)
Ho et al. (2003)	R, DB, VC trial (123)	+		P (3-23 mts)
Reitamo et al. (2009)	R, DB (46)	+		T (3-24 mts)
Schneider et al. (2016)	R, DB (546)	+		P (3-18 mts)
Kaufmann et al. (2004)	R, DB, VC (129)	+		P (3-23 mts)
Level 2 evidence:				
Sigurgeirsson et al. (2015)	OLE (1205)	+	1408	P ~ TCS (infants 3-12 mts)
Staab et al. (2005)	Open, NC trial (22)	+		P (infants 3-23 mts)
Mandelin et al. (2012)	Open, NC trial (50)	+		T (infants <2 yrs)
Housman et al. (2004)	Retrospective CR (38)	+		T (infants <2 yrs)
Patel et al. (2003)	Retrospective CR (12)	+		T (infants <2 yrs)
Lakhanpaul et al. (2006)	Open NC trial (5)	+		P (6-12 mts)
Papp et al. (2005)	OLE (76)	+		P (18-41 mts; 3-24 mts at entry into 1-yr DB trial by Kapp)
Level 3 evidence:				
Other:				
Lebwohl (2017)	Textbook (NA)	+	NA	T (3 rd -line; level B) or P (3 rd -line level A/E)
Lack of effect:				
Evidence of harm:				

C: controlled; DB, double blind; NA: not applicable; NC: noncomparative; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus; TCS: topical corticosteroid; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (atopic dermatitis AND infant)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans
4) Age: infant birth -23 months

Total articles retrieved: 19

- 15 excluded at title/abstract filtering stage:
 - 1 guideline with no specific recommendation on infant AD
 - 1 focused on food allergies in AD
 - 6 AD in children (not infants)
 - 5 AD in mixed populations (not all <2 yrs)
 - 1 meta-analysis does not stratify by age < or > 2
 - 1 no TCI exposure

Selected full citations:

1. Sigurgeirsson B, et al. Safety and efficacy of pimecrolimus in atopic dermatitis: a 5-year randomized trial. *Pediatrics*. 2015;135:597-606.
2. Lee SJ et al. Functional interpretation of metabolomics data as a new method for predicting long-term side effects: treatment of atopic dermatitis in infants. *Sci Rep*. 2014;4:7408.
3. Staab D et al. Low Systemic Absorption and Good Tolerability of Pimecrolimus, Administered as 1% Cream (Elidel®) in Infants with Atopic Dermatitis – A Multicenter, 3-Week, Open-Label Study. *Pediatr Dermatol*. 2005;22:465-71.
4. Papp K et al. Effect of pimecrolimus cream 1% on the long-term course of pediatric atopic dermatitis. *Int J Dermatol*. 2004;43:978-83.

Articles identified through manual searches:

5. Kapp A et al. Long-term management of atopic dermatitis in infants with topical pimecrolimus, a nonsteroid anti-inflammatory drug. *J Allergy Clin Immunol.* 2002;110:277-84.
6. Ho VC et al. Safety and efficacy of nonsteroid pimecrolimus cream 1% in the treatment of atopic dermatitis in infants. *J Pediatr.* 2003;142:155-62.
7. Reitamo S et al. The pharmacokinetics of tacrolimus after first and repeated dosing with 0.03% ointment in infants with atopic dermatitis. *Int J Dermatol.* 2009;48:348-55.
8. Mandelin JM et al. Long-term efficacy and tolerability of tacrolimus 0.03% ointment in infants : a two-year open-label study. *Int J Dermatol.* 2012;51(1):104-10.
9. Housman TS et al. Tacrolimus ointment: utilization patterns in children under age 2 years. *Dermatol Oneline J.* 2004;10(1):2.
10. Patel R et al. The safety and efficacy of tacrolimus therapy in patients younger than 2 years with atopic dermatitis. *Arch Dermatol.* 2003;139(9):1184-6.
11. Lakhapaul M et al. Low systemic exposure in infants with atopic dermatitis in a 1-year pharmacokinetic study with pimecrolimus cream 1%. *Exp Dermatol.* 2006;15(2):138-141.
12. Schneider L et al. Study of the atopic march: development of atopic comorbidities. *Pediatr Dermatol.* 2016;33(4):388-398.
13. Papp KA et al. Long-term control of atopic dermatitis with pimecrolimus cream 1% in infants and young children: A two-year study. *J Am Acad Dermatol.* 2005;52:240-6.
14. Kaufmann R et al. Onset of action of pimecrolimus cream 1% in the treatment of atopic eczema in infants. *J Allergy Clin Immunol.* 2004;114:1183-8.

Balanitis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Georgala et al. (2007)	R, PC trial (11)	+	11	P (non-specific recurrent balanitis)
Level 2 evidence:				
Level 3 evidence: Delgado et al. (2011) Herrera-Esparza (2009) Stinco et al. (2009) Bardazzi et al. (2008) Roé et al. (2007)	Case report (2) Case series (4) Case series (3) Case report (2) Case report (3)	+	22	P (Zoon's plasma cell balanitis) T (refractory circinate balanitis associated with reactive arthritis) P (refractory Zoon's; 1 complete + 2 partial response) P (refractory Zoon's) T (refractory Zoon's)

Chander et al. (2009)	Case report (1)	+		T (Zoon's)
Hague (2006)	Case report (1)	+		T (Zoon's)
Moreno-Arias (2005)	Case report (2)	+		T (Zoon's)
De Almeida (2005)	Case report (2)	+		P (balanitis circinata erosive)
Hernandez-Machin (2005)	Case report (1)	+		T (Zoon's)
Pandher et al. (2003)	Case report (1)	+		T (balanitis xerotica obliterans)
Other: Lebwohl (2017)	Textbook (NA)	+	NA	T (3 rd -line; level B) or P (3 rd -line level A/E)
Lack of effect: Starritt & Lee (2008)	Case report (1)	0	1	P (Zoon's + erythroplasia of Queyrat)
Evidence of harm: Langeland & Engh (2005)	Case report (1)	-	1	T (acceleration of SCC after tx for balanoposthitis)

NA: not applicable; PC, placebo controlled; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (balanitis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 19

- 6 excluded at title/abstract filtering stage:
 - 1 mupirocin therapy
 - 1 dapsone therapy
 - 1 Cochrane review on genital lichen sclerosus (no papers on TCIs for balanitis included)
 - 1 plasma cell cheilitis (lips)
 - 1 case with no mention of TCI outcome
 - 1 plasma cell vulvitis

Selected full citations:

1. Delgado L et al. Zoon's plasma cell balanitis: a report of two cases treated with pimecrolimus. An Bras Dermatol. 2011;86(4 Suppl 1):S35-8.
2. Herrera-Esparza R et al. Tacrolimus therapy for circinate balanitis associated with reactive arthritis. J Clin Rheumatol. 2009;15:377-9.
3. Stinco G et al. Discordant results with pimecrolimus 1% cream in the treatment of plasma cell balanitis. Dermatology. 2009;218:155-8.
4. Starritt E, Lee S. Erythroplasia of Queyrat of the glans penis on a background of Zoon's plasma cell balanitis. Australas J Dermatol. 2008;49:103-5.
5. Bardazzi F et al. Two cases of Zoon's balanitis treated with pimecrolimus 1% cream. Int J Dermatol. 2008;47:198-201.
6. Georgala S et al. Pimecrolimus 1% cream in non-specific inflammatory recurrent balanitis. Dermatology 2007;215:209-12.
7. Roé E et al. Plasma cell balanitis of zoon treated with topical tacrolimus 0.1%: report of three cases. JEADV 2007;21:284-5.
8. Hague J, Ilchyshyn A. Successful treatment of Zoon's balanitis with topical tacrolimus. Int J Dermatol 2006;45:1251-2.
9. Moreno-Arias GA et al. Plasma cell balanitis treated with tacrolimus 0.1%. Br J Dermatol 2005;153:1204-6.
10. de Almeida HL Jr, de Oliveira Filho UL. Topical pimecrolimus is an effective treatment for balanitis circinata erosiva. Int J Dermatol 2005;44:888-9.
11. Hernandez-Machin B et al. Plasma cell balanitis of Zoon treated successfully with topical tacrolimus. Clin Exp Dermatol 2005;30:588-9.
12. Langeland T, Engh V. Topical use of tacrolimus and squamous cell carcinoma on the penis. Br J Dermatol 2005;152:183-5.
13. Pandher BS et al. Treatment of balanitis xerotica obliterans with topical tacrolimus. J Urol 2003;170:923.

Articles identified through manual searches:

14. Chander R et al. Treatment of balanitis of Zoon's with tacrolimus 0.03% ointment. Ind J Sex Transmitted Dis AIDS; 2009;30:56-7.

Behçet's disease

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Chams-Davatchi (2010) Köse et al. (2009)	R, DB, PC trial (45) RCT (38)	+	83	P (genital aphthous ulcers of Behcet's; 18/45 ↓ pain vs 4/45) P (genital ulcers; ↓ pain but not healing time)
Level 2 evidence:				

Level 3 evidence:				
Other: Lebwohl (2017)	Textbook (NA)	+	NA	P or T (1 st -line; Level A)
Lack of effect:				
Evidence of harm:				

DB, double blind; NA: not applicable; PC, placebo controlled; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (behcet)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 14

- 12 excluded at title/abstract filtering stage:
 - 2 cyclosporine therapy
 - 1 Cochrane review cites 1 trial but no data reported (cited as an “additional reference”)
 - 1 no mention of TCI
 - 1 ophthalmic solution of TAC
 - 1 Italian article
 - 4 non-systematic review
 - 1 Cochrane review predates availability of TAC/PIM (2000)
 - 1 blepharoconjunctivitis in rats

Selected full citations:

1. Chams-Davatchi C et al. Pimecrolimus versus placebo in genital aphthous ulcers of Behcet's disease: a randomized double-blind controlled trial. *Int J Rheum Dis* 2010;13:253-8.
2. Köse O et al. Randomized trial of pimecrolimus cream plus colchicine tablets versus colchicine tablets in the treatment of genital ulcers in Behçet's disease. *Dermatology* 2009;218:140-5.

Chronic hand dermatitis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Hordinsky et al. (2010) Krejci-Manwaring (2008) Belsito et al. (2004) Schnopp et al (2002)	R, DB, VC (326) R, DB, VC (21) R, VC trial (151) R, OB, C trial (8)	+	506	P (mild/mod CHD) T + prednisone taper (mod-severe CHD) P (significant benefit in palmar CHD only) T ~ TCS (dyshidrotic palmar eczema)
Level 2 evidence: Schliemann et al. (2007) Thelmo et al. (2003) Thaçi et al. (2003)	Open NC trial (29) Open NC trial (15) Open NC trial (12)	+	56	T (mild-mod occupational hand dermatitis) T (hand and foot eczema; n-value for hand) P (mod-severe CHD)
Level 3 evidence: Bukhari (2005)	Case report (1)	+	1	P (steroid-resistant vesicular CHD)
Other: Lebwohl (2017)	Textbook (NA)	+	NA	P or T (1 st -line; Level C)
Lack of effect:				
Evidence of harm:				

CHD: chronic hand dermatitis; DB, double blind; NA: not applicable; NC: noncomparative; OB: observer-blind; P: pimecrolimus; R, randomized; RCT, randomized controlled trial;

T: tacrolimus; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (chronic hand dermatitis OR pomphylox)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 13

- 6 excluded at title/abstract filtering stage:
 - 1 alitretinoin therapy
 - 1 non-target population (all types of eczema)
 - 1 dishydrrotic palmoplantar eczema
 - 2 cyclosporine therapy
 - 1 allergic contact hand eczema

Selected full citations:

1. Hordinsky M et al. Efficacy and safety of pimecrolimus cream 1% in mild-to-moderate chronic hand dermatitis: a randomized, double-blind trial. *Dermatology* 2010;221:71-7.
2. Krejci-Manwaring J et al. Topical Tacrolimus 0.1% Improves Symptoms of Hand Dermatitis in Patients Treated with a Prednisone Taper. *J Drugs Dermatol* 2008;7(7):643-646.
3. Schliemann S et al. Tacrolimus Ointment in the Treatment of Occupationally Induced Chronic Hand Dermatitis. *Contact Dermatitis* 2008;58(5):299-306.
4. Bukhari IA. Successful Treatment of Chronic Persistent Vesicular Hand Dermatitis with Topical Pimecrolimus. *Saudi Med J* 2005;26(12):1989-1991.
5. Belsito DV et al. Pimecrolimus Cream 1%: A Potential New Treatment for Chronic Hand Dermatitis. *Cutis* 2004;73(1):31-38.
6. Thaçi D et al. Occlusive Treatment of Chronic Hand Dermatitis with Pimecrolimus Cream 1% Results in Low Systemic Exposure, is Well Tolerated, Safe, and Effective. An Open Study. *Dermatology* 2003;207(1):37-42.

7. Schnopp C et al. Topical Tacrolimus (FK506) and Mometasone Furoate in Treatment of Dyshidrotic Palmar Eczema: a Randomized, Observer-blinded Trial. *J Am Acad Dermatol* 2002;46(1):73-77.

Chronic pruritus

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Ucak et al. (2013) Panahi et al. (2008)	R, VC trial (16) R, SB, C trial (35)	+	51	T (pruritus ani) P ~ TCS (chronic pruritis yrs after sulfur mustard exposure)
Level 2 evidence: Sarifakioglu (2006) Kyupers et al. (2004)	Open, NC trial (15) Open, NC trial (25)	+	40	P (chronic vulvar pruritus) T (uraemic pruritus in pts on chronic dialysis)
Level 3 evidence:				
Other: Lebwohl (2017)	Textbook (NA)	+	NA	T (1 st -line for pruritus ani; Level A)
Lack of effect:				
Evidence of harm:				

C: controlled; NA: not applicable; NC: noncomparative; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SB: single blind; T: tacrolimus; TCS: topical corticosteroid

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (chronic pruritus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 39

- 35 excluded at title/abstract filtering stage:

- 1 non-systematic review
- 5 articles on seborrheic dermatitis
- 9 articles on AD
- 3 articles on GVHD
- 6 articles on lichen sclerosus
- 1 article on prurigo nodularis
- 5 articles on chronic irritant/allergic hand dermatitis
- 1 article on balanitis
- 2 articles on external otitis
- 1 article on Pityriasis alba
- 1 article on actinic dermatitis

Selected full citations:

1. Ucak H et al. Efficacy of topical tacrolimus for the treatment of persistent pruritus ani in patients with atopic dermatitis. *J Dermatol Treat* 2013;24:454-7.
2. Panahi Y et al. Comparison of Clinical Efficacy of Topical Pimecrolimus with Betamethasone in Chronic Skin Lesions Due to Sulfur Mustard Exposure: A Randomized, Investigator-Blind Study. *Basic Clin Pharmacol Toxicol* 2008;104:171-5.
3. Sarifakioglu E, Gumus II. Efficacy of topical pimecrolimus in the treatment of chronic vulvar pruritus: a prospective case series--a non-controlled, open-label study. *J Dermatolog Treat* 2006;17:276-8.
4. Kuypers DR et al. A prospective proof of concept study of the efficacy of tacrolimus ointment on uraemic pruritus (UP) in patients on chronic dialysis therapy. *Nephrol Dial Transplant* 2004;19:1895-901.

Contact dermatitis, allergic

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Saripalli et al. (2002) Katsarou et al. (2012) Bhardwaj et al. (2007) Pacor et al. (2006) Belsito et al. (2006) Alomar et al. (2003)	R, DB, VC bilateral (19) RCT (15) RCT (21) R, DB, PC trial (14) R, DB, VC bilateral (98) R, DB, C, bilateral (28)	+	195	T (nickel ACD) T ~ TCS (various allergens) P vs T vs TCS vs TCS (induced nickel ACD) T (steroid-resistant nickel ACD) T (nickel ACD) T (occlusion) > TCS (nickel ACD)
Level 2 evidence: Han et al. (2014)	Open NC trial (82)	+	82	T (various allergens)
Level 3 evidence: Hoverson et al. (2015) Nakada et al. (2005)	Case report (1) Case report (1)	+	2	T (Dermestid allergy; facial lesions tx'd with T; body with TCS) T (prevention of relapse of eyeglass frame ACD)
Other: Lebwohl (2017)	Textbook (NA)	+	NA	P or T (1 st -line; Level B)
Lack of effect: Amrol et al. (2003)	Open, VC, bilateral trial (12)	0	12	P ~ PL (poison ivy rash)
Evidence of harm: Neczyporenko (2010) Saitta (2007) Shaw et al. (2007) Shaw et al. (2004)	Case report (1) Case report (1) Case report (1) Case report (1)	-	4	P (girl treated for AD) P (woman treated for chronic stasis dermatitis) P and T (adolescent pt treated for AD) T (boy treated for AD)

ACD: allergic contact dermatitis; C: controlled; DB, double blind; NA: not applicable; NC: noncomparative; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus; TCS: topical corticosteroid; VC; vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (allergic contact dermatitis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 30

- 16 excluded at title/abstract filtering stage:
 - 2 articles not specific to ACD
 - 3 non-systematic reviews
 - 3 cyclosporine therapy
 - 1 no mention of TCI
 - 1 jellyfish stings
 - 1 French case report not available (Schmutz et al. Ann Dermatol Venereol 2008)
 - 1 study evaluated allergenicity of polypropylene glycol vehicle in PIM
 - 1 case of nodular actinic reticuloid
 - 1 article could not be accessed (Mercader et al. Acta Derm Venereol 2005)
 - 2 cases of chronic actinic dermatitis

Selected full citations:

1. Hoverson K et al. Dermestid Dermatitis in a 2-Year-Old Girl: Case Report and Review of the Literature. *Pediatr Dermatol* 2015;32:e228-33.
2. Han JS et al. Tacrolimus 0.1% ointment in the treatment of allergic contact dermatitis: a new approach. *Int J Dermatol* 2014;53:e470-1.
3. Saripalli YV et al. Tacrolimus ointment 0.1% in the treatment of nickel-induced allergic contact dermatitis. *JAAD* 2003;49:477-82.
4. Katsarou A et al. Tacrolimus 0.1% vs mometasone furoate topical treatment in allergic contact hand eczema: a prospective randomized clinical study. *Eur J Dermatol* 2012;22(2):192-196.
5. Neczyporenko F, Blondeel A. Allergic contact dermatitis to Elidel cream itself? *Contact Dermatitis* 2010;63:171-2.

6. Bhardwaj SS et al. A double-blind randomized placebo-controlled pilot study comparing topical immunomodulating agents and corticosteroids for treatment of experimentally induced nickel contact dermatitis. *Dermatitis* 2007;18:26-31.
7. Saitta P, Brancaccio R. Allergic contact dermatitis to pimecrolimus. *Contact Dermatitis* 2007;56:43-4.
8. Pacor ML et al. Tacrolimus ointment in nickel sulphate-induced steroid-resistant allergic contact dermatitis. *Allergy Asthma Proc* 2006;27:527-31.
9. Shaw DW et al. Allergic contact dermatitis from pimecrolimus in a patient with tacrolimus allergy. *JAAD* 2007;56:342-5.
10. Belsito D et al. A prospective randomized clinical trial of 0.1% tacrolimus ointment in a model of chronic allergic contact dermatitis. *JAAD* 2006;55:40-6.
11. Nakada T et al. Eyeglass frame allergic contact dermatitis: does tacrolimus prevent recurrences? *Contact Dermatitis* 2005;53:219-21.
12. Shaw DW et al. Allergic contact dermatitis from tacrolimus. *JAAD* 2004;50:962-5.
13. Alomar A et al. Topical tacrolimus 0.1% ointment (protopic) reverses nickel contact dermatitis elicited by allergen challenge to a similar degree to mometasone furoate 0.1% with greater suppression of late erythema. *Contact Dermatitis* 2003;49:185-8.
14. Amrol D et al. Topical pimecrolimus in the treatment of human allergic contact dermatitis. *Ann Allergy Asthma Immunol* 2003;91:563-6.

Contact dermatitis, irritant

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Engel et al. (2008)	R, PC, OB trial (36)	+	36	P ~ TCS (SLS-induced irritation)
Level 2 evidence: Jungersted et al. (2011)	Open label trial (19)	+	19	T ~ TCS (\downarrow response to sodium lauryl sulphate irritation)
Level 3 evidence:				
Other: Lebwohl (2017)	Textbook (NA)	+	NA	P or T (1 st -line; Level C)
Lack of effect: Clemmensen et al. (2011)	R, DB, C trial (36)	0	36	T (trend to worsened irritancy of SLS)
Evidence of harm:				

C: controlled; DB, double blind; NA: not applicable; OB: observer-blind; PC, placebo controlled; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SLS: sodium lauryl sulfate; T: tacrolimus; TCS: topical corticosteroid

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (irritant contact dermatitis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 8

- 5 excluded at title/abstract filtering stage:
 - 1 non-systematic review
 - 1 study evaluated allergenicity of propylene glycol vehicle in PIM
 - 3 studies in AD

Selected full citations:

1. Jungersted JM et al. Effects of topical corticosteroid and tacrolimus on ceramides and irritancy to sodium lauryl sulphate in healthy skin. *Acta Derm Venereol* 2011;91(3):290-4.
2. Clemmensen A et al. Applicability of an exaggerated forearm wash test for efficacy of testing two corticosteroids, tacrolimus and glycerol, in topical formulations against skin irritation induced by two different irritants. *Skin Res Technol* 2011;17(1):56-62.
3. Engel K et al. Anti-inflammatory effect of pimecrolimus in the sodium lauryl sulphate test. *J Eur Acad Dermatol Venereol* 2008;22(4):447-450.

Cutaneous lupus erythematosus (CLE)

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs				
Wang et al. (2015) Pothinamthong (2012) Kuhn et al. (2011) Barikbin et al. (2009) Tzung (2007)	RCT (22) RCT (21) R, DB, VC (30) R, DB (5) R, DB, bilateral comp (20)	+	98	T ~ triamcinolone (labial DLE) T < TCS but significantly reduced disease (DLE) T (acute, not sustained relief of CLE) T ~ TCS (facial DLE) T ~ TCS (facial CLE)
Level 2 evidence:				
Heffernan et al. (2005) Tlacuilo-Parra (2005) Kreuter et al. (2004) Lampropoulos (2004)	Open NC trial (5) Open NC trial (10) Open NC trial (11) Open NC trial (12)	+	38	T (DLE) P (DLE) P (CLE; under occlusion) T (resistant CLE)
Level 3 evidence:				
Chen et al. (2018) Milam et al. (2015) Khelifa et al (2011) Kawachi et al. (2011) Del Boz et al. (2008) Cooper et al. (2007) Sugano et al. (2006) Cassis & Callen (2005) De la Rosa (2004) Druke et al. (2004) Kanekura et al. (2003) Zabawski (2002) Walker et al. (2002) Yoshimasu et al. (2002)	Case report (1) Case series (3) Case report (1) Case report (1) Case report (2) Case report (1) Case series (4) Case report (1) Case report (1) Case report (1) Case report (1) Case series (3) Case report (1) Case series (2) Case series (11)	+	33	T + HCQ + prednisolone T 0.3% + oral antimalarial (DLE) T (overlap linear morphea + chronic cutaneous lupus) T (linear childhood DLE) T (childhood DLE) T (childhood periorbital neonatal CLE) T (DLE) T (drug-induced subacute CLE) T (chronic DLE) T (subacute CLE) T (facial CLE) P (facial DLE) T + TCS (chronic severe recalcitrant DLE) T (facial CLE and dermatomyositis; 6/11 response)
Other:				
Jessop et al. (2017) Tzellos et al. (2008) Lebwohl (2017) Bologna (2018)	Cochrane review (14) Systematic review (60) Textbook (NA) Textbook (NA)	+/-	NA	T (primary outcome not measured) P or T (CLE) P or T (1 st -line for DLE; Level B) P or T (based on large case series)
Lack of effect:				
Cakici et al. (2016)	Case report (1)	0	1	T (periorbital discoid lupus)

Evidence of harm:				
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CLE: cutaneous lupus erythematosus; DB, double blind; DLE: discoid lupus erythematosus; HCQ: hydroxychloroquine; NA: not applicable; NC: noncomparative; P: pimecrolimus;

R, randomized; RCT, randomized controlled trial; T: tacrolimus; TCS: topical corticosteroid; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (cutaneous lupus erythematosus OR discoid lupus erythematosus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 37

- 11 excluded at title/abstract filtering stage:
 - 1 IVIG therapy
 - 2 non-systematic reviews
 - 1 no use of TCI reported
 - 1 unable to retrieve full text (Mymensingh Med J)
 - 1 cyclosporine therapy
 - 1 older version of Cochrane review already retrieved
 - 1 molecular profile study
 - 1 case of localized pemphigoid
 - 1 contact dermatitis case
 - 1 letter (no access)

Selected full citations:

1. Chen X et al. A case report of lupus erythematosus tumidus converted from discoid lupus erythematosus. *Medicine (Baltimore)* 2018;97:e0375.
2. Jessop S et al. Drugs for discoid lupus erythematosus. *Cochrane Database Syst Rev* 2017;5:CD002954.
3. Cakici O et al. Periorbital discoid lupus: a rare localization in a patient with systemic lupus erythematosus. *An Bras Dermatol* 2016;91(5 suppl 1):122-4.
4. Milam EC et al. Treatment of Scarring Alopecia in Discoid Variant of Chronic Cutaneous Lupus Erythematosus With Tacrolimus Lotion, 0.3. *JAMA Dermatol* 2015;151:1113-6.
5. Wang X et al. Tacrolimus 0.03% ointment in labial discoid lupus erythematosus: A randomized, controlled clinical trial. *J Clin Pharmacol* 2015;55:1221-8.
6. Pothinamthong P, Janjumratsang P. A comparative study in efficacy and safety of 0.1% tacrolimus and 0.05% clobetasol propionate ointment in discoid lupus erythematosus by modified cutaneous lupus erythematosus disease area and severity index. *J Med Assoc Thai* 2012;95:933-40.
7. Khelifa E et al. Linear sclerodermic lupus erythematosus, a distinct variant of linear morphea and chronic cutaneous lupus erythematosus. *Int J Dermatol* 2011;50:1491-5.
8. Kuhn A et al. Efficacy of tacrolimus 0.1% ointment in cutaneous lupus erythematosus: a multicenter, randomized, double-blind, vehicle-controlled trial. *JAAD* 2011;65:54-64.
9. Kawachi Y et al. Linear childhood discoid lupus erythematosus following the lines of Blaschko: successfully treated with topical tacrolimus. *Pediatr Dermatol* 2011;28:205-7.
10. Barikbin B et al. Pimecrolimus 1% cream versus betamethasone 17-valerate 0.1% cream in the treatment of facial discoid lupus erythematosus: a double-blind, randomized pilot study. *Clin Exp Dermatol* 2009;34:776-80.
11. Del Boz J et al. Childhood discoid lupus in identical twins. *Pediatr Dermatol* 2008;25:648-9.
12. Tzellos TG, Kouvelas D. Topical tacrolimus and pimecrolimus in the treatment of cutaneous lupus erythematosus: an evidence-based evaluation. *Eur J Clin Pharmacol* 2008;64:337-41.
13. Cooper RM et al. Periorbital cutaneous neonatal lupus. *Skinmed* 2007;6:145-6.
14. Tzung TY et al. Tacrolimus vs. clobetasol propionate in the treatment of facial cutaneous lupus erythematosus: a randomized, double-blind, bilateral comparison study. *Br J Dermatol* 2007;156:191-2.
15. Sugano M et al. Successful treatment with topical tacrolimus in four cases of discoid lupus erythematosus. *J Dermatol* 2006;33:887-91.
16. Cassis TB, Callen JP. Bupropion-induced subacute cutaneous lupus erythematosus. *Australas J Dermatol* 2005;46:266-9.
17. Heffernan MP et al. 0.1% tacrolimus ointment in the treatment of discoid lupus erythematosus. *Arch Dermatol* 2005;141:1170-1.
18. Tlacuilo-Parra A et al. Pimecrolimus 1% cream for the treatment of discoid lupus erythematosus. *Rheumatology (Oxford)* 2005;44:1564-8.

19. Kreuter A et al. Pimecrolimus 1% cream for cutaneous lupus erythematosus. JAAD 2004;51:407-10.
20. Lampropoulos CE et al. Topical tacrolimus therapy of resistant cutaneous lesions in lupus erythematosus: a possible alternative. Rheumatology (Oxford) 2004;43:1383-5.
21. de la Rosa Carrillo D, Christensen OB. Treatment of chronic discoid lupus erythematosus with topical tacrolimus. Acta Derm Venereol 2004;84:233-4.
22. Duke A et al. 0.1% Tacrolimus ointment in a patient with subacute cutaneous lupus erythematosus. J Dermatolog Treat 2004;15:63-4.
23. Kanekura T et al. Efficacy of topical tacrolimus for treating the malar rash of systemic lupus erythematosus. Br J Dermatol 2003;148:353-6.
24. Zabawski E. Treatment of cutaneous lupus with Elidel. Dermatol Online J 2002;8:25.
25. Walker SL et al. The effect of topical tacrolimus on severe recalcitrant chronic discoid lupus erythematosus. Br J Dermatol 2002;147:405-6.
26. Yoshimasu T et al. Topical FK506 (tacrolimus) therapy for facial erythematous lesions of cutaneous lupus erythematosus and dermatomyositis. Eur J Dermatol 2002;12:50-2.

Keratosis pilaris

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Breithaupt et al. (2011)	DB paired comparison (30)	+	30	T > Aquaphor ointment (children age 2-16)
Level 2 evidence:				
Level 3 evidence:				
Other: Lebwohl (2017)	Textbook (NA)	+	NA	T (2 nd -line; Level A)
Lack of effect:				
Evidence of harm:				

DB, double blind; NA: not applicable; P: pimecrolimus; RCT, randomized controlled trial; T: tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (keratosis pilaris)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 3

- 2 excluded at title/abstract filtering stage:
 - 1 eccrine squamous metaplasia
 - 1 non-study population (frontal fibrosing alopecia)

Selected full citations:

1. Breithaupt AD et al. A comparative trial comparing the efficacy of tacrolimus 0.1% ointment with Aquaphor ointment for the treatment of keratosis pilaris. Pediatr Dermatol 2011;28:459-60.

Lichen planus (oral, mucosal, erosive, esophageal, nail, cutaneous, pigmentosus, planopilaris, facial actinic; *excluded genital*)

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: meta-analyses Chamani et al (2015) Guo et al. (2015)	Meta-analysis (NA) Meta-analysis (476)	+	>476	T > TCS (OLP) T~TCS (erosive OLP)
Level 1 evidence: RCTs Siponen et al (2017) Hettiarachchi et al (2017) Vohra et al. (2016) Arduino et al. (2014)	R, DB, PC trial (11) R, DB, C trial (34) RCT (40) R, DB, C trial (30)	+	240	T ~ triamcinolone acetonide (OLP) T ~ TCS (OLP) P ~ T (OLP) P or T (unresponsive OLP)

Sonthalia (2012)	R, DB trial (20)	+		T vs TCS (OLP)
Volz et al. (2008)	R, DB, VC (10)	+		P (eruptive OLP)
Corrocher et al. (2008)	R, DB, C (16)	+		T > TCS (OLP)
Radfar et al. (2008)	R, DB, C (15)	+		T ~ TCS (OLP)
Gorouhi et al. (2007)	R, SB, C (18)	+		P ~ TCS (OLP)
Passeron et al. (2007)	R, DB, PC (6)	+		P (eruptive OLP)
Laeijendecker et al. (2006)	R, C trial (20)	+		T > TCS (OLP)
Swift et al. (2005)	R, PC trial (10)	+		P (eruptive OLP)
Singh et al. (2017)	R, OL, C trial (10)	+		T vs TCS vs dapsone vs retinoid (OLP)
Level 2 evidence:				
McCaughay et al. (2011)	OLE (10)	+	71	P (OLP)
Al-Mutairi (2010)	Open NC trial (13)	+		T (LP pigmentosus)
Tavassol et al (2008)	Open NC trial (11)	+		T (OLP)
Lozada-Nur (2006)	Open NC trial (10)	+		T (LP or OLP)
Olivier et al (2002)	Open NC trial (8)	+		T (chronic eruptive OLP)
Kaliakatsou et al. (2002)	Open NC trial (19)	+		T (eruptive or ulcerative OLP)
Level 3 evidence:				
Sugashima (2012)	Case report: T (1)	+	42	T (annular LP of the lip)
Cañadas et al (2010)	Case report: T (1)	+		T (linear lichen planopilaris of the face)
Sälävästru & Tiplica (2010)	Case report: T (1)	+		T (ulcerative LP)
Ujiie et al (2010)	Case series: T (5)	+		T (nail LP)
Fontina et al (2008)	Case report: T(1)	+		T (LP child)
Blazek & Megahed (2008)	Case report: T (1)	+		T (lichen planopilaris)
Ezzedine et al (2009)	Case report: P (1)	+		T (facial actinic LP)
Al-Khenaizan (2008)	Case report: T (1)	+		T (ulcerative LP of the sole)
Rabanal et al (2007)	Case report : T (1)	+		T (Severe eruptive OLP)
Erkek et al (2007)	Case report: T & P (1)	+		P + T (OLP)
Riano Arguelles et al (2006)	Case report: T (1)	+		T (eruptive OLP)
Petropoulou et al (2006)	Case report: T (1)	+		T + thalidomide (eruptive LP)
Domínguez et al (2006)	Case series: T (2)	+		T (linear LP and Hepatitis C)
Sichinohe et al (2006)	Case report: T (1)	+		T (severe recalcitrant eruptive OLP)
Donovan et al (2005)	Case report: T (1)	+		T (refractory eruptive OLP and Hepatitis C)
Meyer et al (2005)	Case report: T (1)	+		T (eruptive LP)
Eisman & Orteu (2004)	Case series: P (3)	+		T + thalidomide (recalcitrant eruptive flexural LP)
Esquivel-Pedraza (2004)	Case series: T (6)	+		P (OLP)
Morrison et al (2002)	Case report: T (1)	+		T (eruptive OLP)
Lener et al (2001)	Case series: T (6)	+		T (eruptive LP)
				T (eruptive mucosal LP)

Vente et al (1999) Kim et al (2012) Dissemond (2008) Chaudhry (2007) Dissemond et al (2004)	Case report (1) Case report (1) Case report (1) Case report (1) Case report (1)	+		T + neodymium:yttrium -Al-garnet laser (LP pigmentosus) P (OLP) T (recalcitrant OLP) P (OLP)
Other: Davari et al (2014) Elad et al. (2010) Al Johani et al. (2009) Cheng et al. (2012) Lebwohl (2017) Bologna (2018)	Systematic review (NA) Systematic review (107) Systematic review (>240) Cochrane SR (41) Textbook (NA) Textbook (NA)	+	>388	P or T (2 nd -line for MLP, steroid-sparing) P or T (2 nd -line for OLP; Level 2b/c) P or T (2 nd -line for OLP; T > P) P or T (weak evidence for OLP) P or T (3 rd line; Level E) P or T (OLP: level 1; vulvovaginal: level 2; other: level 3)
Lack of effect: Lodi et al. (2012) Kim et al. (2008)	Systematic review (82) Case report (1)	0 0	83	P ~ PL, T ~TCS (OLP pain) T (and TCS; pt with LP and LP pigmentosus-inversus)
Evidence of harm: Morita et al (2017) Mattson et al (2010) Becker et al (2006) Fricain et al (2005) Shen & Pedvis-Leftick (2004)	Case report : T (1) Case report: T (1) Case report: T (1) Case report: T (1) Case report: T (1)	- - - - -	5	T (carcinoma; OLP pt) T (SCC; OLP pt) T (SCC; OLP pt; prior systemic therapies) T (mucosal pigmentation; OLP pt) T (mucosal staining; erosive OLP pt)

C: controlled; DB, double blind; LP: lichen planus; MLP: mucosal lichen planus; NA: not applicable; NC: noncomparative; OL: open label; OLP: oral lichen planus; PC, placebo controlled; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SB: single blind; SCC: squamous cell carcinoma; SR: systematic review; T: tacrolimus; TCS: topical corticosteroid; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (lichen planus)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 119

- 55 excluded at title/abstract filtering stage:
 - 15 articles on cyclosporine therapy
 - 3 articles on lichen striatus
 - 1 article on lichen sclerosus
 - 1 article on epidermolytic hyperkeratosis
 - 1 article on lichen amyloidosis
 - 4 non systematic reviews
 - 9 articles report no TCI use
 - 1 article on vulvovaginal-gingival syndrome
 - 1 article on plasma cell cheilitis
 - 1 article on frontal fibrosing alopecia
 - 1 case report with no outcome presented (patient was 'lost' to follow up)
 - 1 article was the same systemic review as Lodi et al 2011.
 - 1 article on diltiazem-associated photodistributed hyperpigmentation
 - 1 article on pemphigus vulgaris
 - 1 article on frontal fibrosing alopecia
 - 1 article on describes prior nonresponse to TAC
 - 1 article on graft- versus -host disease
 - 1 article with no access
 - 1 nonanalytic satisfaction survey
 - 1 case of alitretinoin in patient with prior nonresponse to TAC
 - 1 summary of Lodi systematic review
 - 7 articles specific to genital lichen planus (moved to that specific table)

Selected full citations

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2. Hettiarachchi PVKS et al. Comparison of topical tacrolimus and clobetasol in symptomatic oral lichen planus: A double-blinded, randomized clinical trial in Sri Lanka. *J Investig Clin Dent* 2017;8(4):e12237.
3. Chamani G et al. Efficacy of tacrolimus and clobetasol in the treatment of oral lichen planus: a systematic review and meta-analysis. *Int J Dermatol* 2015;54(9):996-1004.
4. Vohra S et al. Clinical and serological efficacy of topical calcineurin inhibitors in oral lichen planus: a prospective randomised controlled trial. *Int J Dermatol* 2016;55(1):101-105.
5. Davari P et al. Mucosal lichen planus: an evidence –based treatment update. *Am J Clin Dermatol* 2014; 15(3):181-195.
6. Arduino PG et al. Pimecrolimus vs. tacrolimus for the topical treatment of unresponsive oral erosive lichen planus: an 8 week randomized double-blind controlled study. *JEADV* 2014;28:475-82.
7. Sonthalia S, Singal A. Comparative efficacy of tacrolimus 0.1% ointment and clobetasol propionate 0.05% ointment in oral lichen planus: a randomized double-blind trial. *Int J Dermatol* 2012;51(11):1371-1378.
8. Elad S et al. Topical immunomodulators for management of oral mucosal conditions, a systematic review; part 1: calcineurin inhibitors. *Expert Opin Emerg Drugs* 2010;15(4):713-726.
9. Al Johani KA et al. Calcineurin inhibitors in oral medicine. *J Am Acad Dermatol* 2009;61(5):829-840.
10. Volz T et al. Pimecrolimus cream 1% in erosive oral lichen planus- a prospective randomized double blind vehicle controlled study. *Br J Dermatol* 2008; 159(4):936-941.
11. Corrocher G et al. Comparative effect of tacrolimus 0.1% ointment and clobetasol 0.05% ointment in patients with oral lichen planus. *J Clin Periodontol* 2008;35(3):244-249.
12. Radfar L et al. A comparative treatment study of topical tacrolimus and clobetasol oral lichen planus. *Oral Surg Med Oral Pathol Oral Radiol Endod* 2008; 105(2):187-193.
13. Goroughi F et al. Randomized trial of pimecrolimus cream versus triamcinolone acetonide paste in the treatment of oral lichen planus. *J Am Acad Dermatol* 2007;57(5):806-813.
14. Passeron T et al. Treatment of oral erosive lichen planus with 1% pimecrolimus cream: a double blind, randomized, prospective trial with measurement of pimecrolimus levels in the blood. *Arch Dermatol* 2007; 143(4):472-476.
15. Laeijendecker R et al. A comparison of treatment of oral lichen planus with topical tacrolimus and triamcinolone acetonide ointment. *Acta Derm Venereol* 2006;86(3):227-229.
16. Swift JC et al. The effectiveness of 1% pimecrolimus cream in the treatment of oral erosive lichen planus. *J Periodontol* 2005;76(4):627-635.
17. Singh AR et al. Efficacy of steroid vs non-steroidal agents in oral lichen planus: a randomised, open –label study. *J Laryngol Otol* 2017;131(1):69-76.
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19. Cheng S et al. Interventions for erosive lichen planus affecting mucosal sites. Cochrane Database Syst Rev 2012;15(2):CD008092.
20. Lodi G et al. Interventions for treating oral lichen planus: a systematic review. Br J Dermatol 2012;166(5):938-947.
21. Keenan AV, Ferraiolo D. Insufficient evidence for effectiveness of any treatment for oral lichen planus. Evid Based Dent 2011;12:85-6.
22. McCaughey C et al. 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 . JEADV 2011;25:1061-7.
23. Al-Mutairi N, El-Khalawany M. Clinicopathological characteristics of lichen planus pigmentosus and its response to tacrolimus ointment: an open label, non-randomized, prospective study. J Eur Acad Dermatol Venereol 2010; 24(5):535-540.
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25. Lozada-Nur FI, Sroussi HY. Tacrolimus powder in Orabase 0.1% for the treatment of oral lichen planus and oral lichenoid lesions: an open clinical trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102(6):744-749.
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32. Fontina AB et al. Topical tacrolimus in the treatment of lichen planus in a child. Pediatr Dermatol 2008;25(5):570-571.
33. Blazek C, Megahed M. Lichen planopilaris. Successful treatment with tacrolimus. Hautart 2008;59(11):874-877.
34. Ezzedine K et al. Facial actinic lichen planus following the Blaschko's lines: successful treatment with topical 0.1% pimecrolimus cream. J Eur Acad Dermatol Venereol 2009;23(4):458-459.
35. Al-Khenaini S, Al Mubarak L. Ulcerative lichen planus of the sole: excellent response to topical tacrolimus. Int J Dermatol 2008;47(6):626-628.
36. Rabanal A et al. Management of a patient with severe erosive lichen planus in need of an immediate complete denture: a clinical report. J Prosthet Dent 2007; 98(4):256-259.
37. Erkek E et al. A case of cheilitis glandularis superimposed on oral lichen planus: successful palliative treatment with topical tacrolimus and pimecrolimus. J Eur Acad Dermatol Venereol 2007;21(7):999-1000.
38. Riano Arguelles A et al. Topical tacrolimus, alternative treatment for oral erosive lichen planus resistant to steroids: a case report. Med Oral Pathol Oral Cir Bucal 2006;11(6):e462-466.

39. Petropoulou H et al. Effective treatment of erosive lichen planus with thalidomide and topical tacrolimus. *Int J Dermatol* 2006; 45(10):1244-1245.
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45. Esquivel-Pedraza I et al. Treatment of oral lichen planus with topical pimecrolimus 1% cream. *Br J Dermatol* 2004;150(4):771-773.
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48. Vente C, Reich K, Ruppercht R et al. Erosive mucosal lichen planus: response to topical treatment with tacrolimus. *Br J Dermatol* 1999;140(2):338-342.
49. Morita M et al. The onset risk of carcinoma in patients continuing tacrolimus topical treatment for oral lichen planus: a case report. *Odontology* 2017;105(2):262-266.
50. Mattson U et al. Squamous cell carcinoma in a patient with oral lichen planus treated with topical application of tacrolimus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010; 110(1):e19-25.
51. Becker JC et al. The carcinogenic potential of tacrolimus ointment beyond immune suppression: a hypothesis creating case report. *BMC Cancer* 2006;11(6):7.
52. Fricain JC et al. Mucosal pigmentation after oral lichen planus treatment with topical tacrolimus. *Dermatology* 2005;210(3):229-232.
53. Shen JT, Pedvis-Leftick A. Mucosal Staining after using topical tacrolimus to treat erosive oral lichen planus. *J Am Acad Dermatol* 2004; 50(2):326.
54. Kim J-E et al. Linear lichen planus pigmentosus of the forehead treated by neodymium:yttrium–aluminum–garnet laser and topical tacrolimus. *J Dermatol* 2011;39:189-191.
55. Dissemont J. Pimecrolimus in an adhesive ointment is safe and effective in long-term treatment for oral lichen planus. *JEADV* 2008;22:1009-11.

56. Kim BS et al. Coexistence of classic lichen planus and lichen planus pigmentosus-inversus: resistant to both tacrolimus and clobetasol propionate ointments. JEADV 2008;22:106-7.
57. Chaudhry et al. The use of topical calcineurin inhibitors in the management of oral lichen planus. JEADV 2007;21:554-6.
58. Dissemond et al. Pimecrolimus in an adhesive ointment as a new treatment option for oral lichen planus. Br J Dermatol 2004;150:782-4.

Lichen sclerosus

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: MA Chi et al. (2012)	SR and MA (38)	+	38	P (but less effective than TCS; vulvar LS)
Level 1 evidence: RCTs Funaro et al. (2014) Goldstein et al. (2011)	R, DB, C (28) R, DB, C (18)	+	46	T < TCS (but improved from baseline; vulvar LS) P (~ TCS for symptoms, < TCS for inflammation; vulvar LS)
Level 2 evidence: Ebert et al. (2008) Oskay et al. (2006) Hengge et al. (2006)	Open, NC trial (20) Open, NC trial (16) Open, NC, Phase 2 trial (84)	+	120	T (adjuvant to surgery; genital LS in boys) P (vulvar LS) T (mostly anogenital LS)
Level 3 evidence: Jimbo et al (2016) Valdivielso-Ramos (2008) Wakamatsu et al. (2008) Kortekangas (2007) Matsumoto (2007) Ginarte & Toribio (2005) Goldstein et al. (2004) Bohm et al. (2003) Kinstfeld et al. (2003) Assmann et al. (2003) Boms et al. (2004)	Case report (1) Case report (1) Case report (1) Case series (3) Case report (1) Case report (1) Case report (1) Case report (1) Case series (6) Case report (1) Case report (1) Case series (4)	+	21	T (LS of the cheek) T + NB-UVB (extravaginal LS) T (LS of the lip) T + MTX (vulvar LS) T (vulvar LS in a child) T (vulvar LS) P (vulvar LS in premenarchal girl refractory to TCS) T (anogenital LS) T (vulvar LS) T (vulvar LS) P (anogenital LS in childhood)
Other: Bercaw-Pratt (2014) Lopez-Perez (2013)	Guideline (NA) Guideline (NA)	+	>17	P or T for pediatric LS nonresponsive to TCS (Level II-3b) P or T (2 nd -line; vulvar LS)

Chi et al. (2011) Lebwohl (2017) Bologna (2018)	Cochrane review (17) Textbook (NA) Textbook (NA)	+		P (~ TCS for symptoms, < TCS for inflammation; vulvar LS) P or T (2 nd -line for LS; Level A/B respectively) P or T ("some efficacy"; risk of reactivation of HPV, SCC)
Lack of effect: Mann et al. (2010) Arican et al. (2004)	Case report (1) Case report (1)	0 0	2	T + topical triamcinolone (folliculocentric LS) P (extragenital LS)
Evidence of harm: Feito-Rodriguez (2014) Kim & Kang (2007) Fischer & Bradford (2007) Bilenchini et al. (2007)	Case report (1) Case report (1) Case report (1) Case report (2)	- - - -	5	T (bacterial vaginosis; pt treated for vulvar LS) T (pigmentation; LS of cheek) T (SCC after tx for vulvar LS and genital psoriasis) T (HPV condylomatosis after tx of anogenital LS)

C: controlled; DB, double blind; HPV: human papillomavirus; LS: lichen sclerosus; MA: meta-analysis; NA: not applicable; NB-UVB: narrow-band ultraviolet B radiation; NC: noncomparative; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SB: single blind; SCC: squamous cell carcinoma; SR: systematic review; T: tacrolimus; TCS: topical corticosteroid; tx: treatment

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (lichen sclerosus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 30

- 5 excluded at title/abstract filtering stage:
 - 2 non-systematic review
 - 1 no TCI outcome reported
 - 1 lichen striatus
 - 1 case of pemphigoid

Selected full citations:

1. Jimbo H et al. Telangiectatic lichen sclerosus on the cheek successfully treated with topical tacrolimus. *Eur J Dermatol* 2016;26:321-2.
2. Funaro D et al. A double-blind, randomized prospective study evaluating topical clobetasol propionate 0.05% versus topical tacrolimus 0.1% in patients with vulvar lichen sclerosus. *JAAD* 2014;71:84-91.
3. Bercaw-Pratt JL et al. Clinical recommendation: pediatric lichen sclerosus. *J Pediatr Adolesc Gynecol* 2014;27:111-6.
4. Feito-Rodriguez M et al. Bacterial vaginosis in the context of lichen sclerosus in a prepubertal girl. *Pediatr Dermatol* 2014;31:95-98.
5. Perez-Lopez FR; EMAS Spanish Menopause Society. EMAS clinical guide: vulvar lichen sclerosus in peri and postmenopausal women. *Maturitas* 2013;74:279-82.
6. Chi CC et al. Systematic review and meta-analysis of randomized controlled trials on topical interventions for genital lichen sclerosus. *JAAD* 2012;67:305-12.
7. Chi CC et al. Topical interventions for genital lichen sclerosus. *Cochrane Database Syst Rev* 2011;(12):CD008240.
8. Goldstein A et al. A double-blind, randomized controlled trial of clobetasol versus pimecrolimus in patients with vulvar lichen sclerosus. *JAAD* 2011;64:e99-104.
9. Mann DJ et al. Folliculocentric lichen sclerosus et atrophicus. *Skinmed* 2010;8 :242-4.
10. Valdivielso-Ramos M et al. Significant improvement in extensive lichen sclerosus with tacrolimus ointment and PUVA. *Am J Clin Derm* 2008;9:175-9.
11. Ebert AK et al. Safety and Tolerability of Adjuvant Topical Tacrolimus Treatment in Boys with Lichen Sclerosus: A Prospective Phase 2 Study. *Eur Urol* 2008;54:932-7.
12. Wakamatsu et al. Lichen sclerosus et atrophicus of the lip: successful treatment with topical tacrolimus. *JEADV* 2008;22:760-2.
13. Kim YJ, Kang HY. Pigmentation after using topical tacrolimus to treat lichen sclerosus: possible role of stem cell factor. *JAAD* 2007;57(5 Suppl):S125-7.
14. Fischer G, Bradford J. Topical immunosuppressants, genital lichen sclerosus and the risk of squamous cell carcinoma: a case report. *J Reprod Med* 2007;52:329-31.
15. Oskay T et al. Pimecrolimus 1% cream in the treatment of vulvar lichen sclerosus in postmenopausal women. *Int J Dermatol* 2007;46:527-32.
16. Kortekangas-Savolainen O, Kiilholma P. Treatment of vulvovaginal erosive and stenosing lichen planus by surgical dilatation and methotrexate. *Acta Obstet Gynecol Scand* 2007;86:339-43.
17. Matsumoto Y et al. Successful treatment of vulvar lichen sclerosus in a child with low-concentration topical tacrolimus ointment. *J Dermatol* 2007;34:114-6.

18. Bilenchi R et al. Human papillomavirus reactivation following topical tacrolimus therapy of anogenital lichen sclerosus. Br J Dermatol 2007;156:405-6.
19. Hengge U et al. Multicentre, phase II trial on the safety and efficacy of topical tacrolimus ointment for the treatment of lichen sclerosus. Br J Dermatol 2006;155:1021-8.
20. Ginarte M, Toribio J. Vulvar lichen sclerosus successfully treated with topical tacrolimus. Eur J Obstet Gynecol 2005;123:123-4.
21. Arican O et al. Unsuccessful treatment of extragenital lichen sclerosus with topical 1% pimecrolimus cream. J Dermatol 2004;31:1014-7.
22. Goldstein AT et al. Pimecrolimus for the treatment of vulvar lichen sclerosus in a premenarchal girl. J Pediatr Adolesc Gynecol 2004;17:35-7.
23. Kunstfeld R et al. Successful treatment of vulvar lichen sclerosus with topical tacrolimus. Arch Dermatol 2003;139:850-2.
24. Assmann T et al. Tacrolimus ointment for the treatment of vulvar lichen sclerosus. JAAD 2003;48:935-7.
25. Bohm M et al. Successful treatment of anogenital lichen scleratosus with topical tacrolimus. Arch Dermatol 2003;139:922-4.

Articles identified through a manual search:

26. Boms S et al. Pimecrolimus 1% cream for anogenital lichen sclerosus in childhood. BMC Dermatol 2004;4:14.

Morphea (localized scleroderma)

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Kroft et al. (2009)	R, DB, PC trial (10)	+	10	T (active plaque morphea)
Level 2 evidence: Stefanaki et al. (2008) Mancuso (2005)	Open NC trial (13) Open NC trial (7)	+	20	T (without occlusion) T (with occlusion)
Level 3 evidence: Trivedi et al. (2017) Cantisani et al. (2013) Khelifa et al (2011) Clark et al. (2010) Mancuso (2003)	Case report (1) Case report (1) Case report (1) Case report (2) Case report (2)	+	7	T + TCS (radiation-induced morphea) T (without occlusion; generalized morphea) T (overlap linear morphea + chronic cutaneous lupus) T (morphea of the breast) T (under occlusion)
Other: Zwischenberger (2011)	Systematic review (21)	+	21	T (Level 2 evidence)

Lebwohl (2017) Bologna (2018)	Textbook (NA) Textbook (NA)	+		T (under occlusion; Level C) T (support from case series)
Lack of effect:				
Evidence of harm: Bhari et al. (2017) Chu et al. (2017)	Case report (1) Case report (1)	- -	2	T (dermatophyte infection after tx for morphea) T (radiation recall dermatitis)

DB, double blind; NA: not applicable; NBNC: noncomparative; PC, placebo controlled; pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (morphea OR localized scleroderma)

Filters: None applied

Total articles retrieved: 18

- 7 excluded at title/abstract filtering stage:
 - 3 non-systematic reviews
 - 1 case series; no outcomes reported
 - 1 review focused on pregnancy outcomes in pts with connective tissue diseases
 - 1 article in German
 - 1 no mention of TCI treatment

Selected full citations:

1. Trivedi A et al. Radiation-induced circumscribed superficial morphea after brachytherapy for endometrial adenocarcinoma. *Int J Womens Dermatol* 2017;3:234-36.
2. Bhari N et al. Tacrolimus induced dermatophyte infection overlying a plaque morphea. *Dermatol Ther* 2017;30(1). pii: 10.1111/dth.12395.
3. Chu CH et al. Radiation recall dermatitis induced by topical tacrolimus for post-irradiation morphea. *JEADV* 2017;31:e80-81.
4. Cantisani C et al. Generalized morphea successfully treated with tacrolimus 0.1% ointment. *J Drugs Dermatol* 2013;12:14-15.

5. Khelifa E et al. Linear sclerodermic lupus erythematosus, a distinct variant of linear morphea and chronic cutaneous lupus erythematosus. *Int J Dermatol* 2011;50:1491-5.
6. Zwischenberger BA, Jacobe HT. A systematic review of morphea treatments and therapeutic algorithm. *JAAD* 2011;65:925-41.
7. Clark CJ, Wechter D. Morphea of the breast – an uncommon cause of breast erythema. *Am J Surg* 2010;200:173-6.
8. Kroft EB et al. Efficacy of topical tacrolimus 0.1% in active plaque morphea: randomized, double-blind, emollient-controlled pilot study. *Am J Clin Dermatol* 2009;10:181-7.
9. Stefanaki C et al. Topical tacrolimus 0.1% ointment in the treatment of localized scleroderma. An open label clinical and histological study. *J Dermatol* 2008;35:712-8.
10. Mancuso G, Berdondini RM. Localized scleroderma: response to occlusive treatment with tacrolimus ointment. *Br J Dermatol* 2005;152:180-2.
11. Mancuso G, Berdondini RM. Topical tacrolimus in the treatment of localized scleroderma. *Eur J Dermatol* 2003;13:590-2.

Pemphigus, bullous pemphigoid, mucus membrane pemphigoid

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Iraji et al (2010) Nazemi et al (2012)	R, DB, C trial (11) R, SB, C trial (15)	+	26	P (adjunctive to systemic steroid + AZA) T ~TCS (oral pemphigus vulgaris)
Level 2 evidence:				
Level 3 evidence : Calcaterra et al (2009) Demistet al (2009) Cohen et al (2006) Cassano et al (2006) Michel & Gain (2006) Wenzel et al (2005) Lebeau et al (2004) Gach & Ichyshyn (2004) Assmann et al (2004) Chu et al (2003)	Case report (1) Case series (3) Case series (2)		17	T (pretibial bullous) T (localized Brunsting-Perry type) T ~ TCS (pemphigus foliaceus) T (recalcitrant pemphigus foliaceous at a surgical site) T (ocular cicatricial pemphigoid) T (bullosus) T (localized childhood vulval pemphigoid) T (recalcitrant pemphigus vulgaris) T (oral cicatrical pemphigoid) T (adjunctive to systemic therapies; bullous)

Hodgson et al (2003) Kim et al. (2008) Chuh et al. (2004) Ko & Chu (2003)	Case report (1) Case report (1) Case report (1) Case report (1)			T (recalcitrant labial pemphigus vulgaris) T (adjuvant to Abx + TCS + chlorhexidine; pemphigus vegetans) T (adjuvant to prednisone; vesicular pemphigoid) T (bulous)
Other: Zhao et al. (2015) Bologna (2018)	Systematic review (26) Textbook (NA)	+	26	P (promising); T (inconclusive) (pemphigus vulgaris) T (based on case series)
Evidence of harm				
Lack of effect				

C: controlled; CHD: chronic hand dermatitis; DB, double blind; NA: not applicable; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SB: single blind; T: tacrolimus; TCS: topical corticosteroid

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (Pemphigus, bullous pemphigoid, mucus membrane pemphigoid)

Filters:

- 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
- 2) Language: English, French
- 3) Species: Humans

Total articles retrieved: 38

- 21 excluded at title/abstract filtering stage:

- 1 articles cyclosporine therapy
- 12 articles on Hailey-Hailey
- 2 non-systematic reviews
- 2 articles reported no TCI use
- 1 animal study
- 1 article on erosive stomatitis
- 1 article on dermatomyositis
- 1 article with no access

Selected full citations:

1. Iraji F et al. Pimecrolimus 1% cream in the treatment of cutaneous lesions of pemphigus vulgaris: a double-blind, placebo controlled clinical trial. *J Drugs Dermatol* 2010;9(6):684-686.
2. Calcaterra R et al. Topical tacrolimus treatment for localized pretibial bullous pemphigoid. *J Eur Acad Dermatol Venereol* 2009;23(2):177-179.
3. Demitsu T et al. Localized pemphigoid (Brunsting-Perry type) with IgG antibody to BP180 NC16a domain resembling lupus erythematosus successfully treated with topical tacrolimus therapy. *J Eur Acad Dermatol Venereol* 2009;23(1):79-80.
4. Cohen SN et al. Equal efficacy of topical tacrolimus and clobetasone butyrate in pemphigus foliaceus. *Int J Dermatol* 2006;45(11):1379
5. Cassano N et al. Recalcitrant lesions of pemphigus foliaceous at a surgical site: successful treatment with tacrolimus 0.1% ointment. *Eur J Dermatol* 2006;16(4):443-434.
6. Michel JL, Gain P. Topical tacrolimus treatment for ocular cicatricial pemphigoid. *Ann Dermatol Venereol* 2006;133(2):161-164.
7. Wenzel J et al. Topical treatment of bullous pemphigoid with tacrolimus. Case report with brief review of the literature. *J Dtsch Dermatol Ges* 2005;3(3):207-210.
8. Termeer CC et al. Topical tacrolimus (Protopic) for the treatment of localized pemphigus foliaceus. *J Eur Acad Dermatol Venereol* 2004;18(5):636-637.
9. Lebeau S et al. Localized childhood vulval pemphigoid treatment with tacrolimus ointment. *Dermatology* 2004;208(3):273-275.
10. Gach JE, Ilchyshyn A. Beneficial effects of topical tacrolimus on recalcitrant erosions of pemphigus vulgaris. *Clin Exp Dermatol* 2004;29(3):271-272.
11. Assmann T et al. Topical Immunomodulators: a therapeutic option for oral cicatricial pemphigoid. *Hautarzt* 2004;55(4):390-392.
12. Chu J et al. Topical tacrolimus is a useful adjunctive therapy for bullous pemphigoid. *Arch Dermatol* 2003;139(6):813-815.

13. Hodgson TA et al. Topical tacrolimus: a novel therapeutic intervention for recalcitrant labial pemphigus vulgaris. *Eur J Dermatol* 2003; 13(2):142-144.
14. Zhao CY, Murrell DF. Pemphigus vulgaris: An evidence-based treatment update. *Drugs* 2015;75:271-84.
15. Kim J et al. Pemphigoid vegetans: a case report and review of the literature. *J Cutan Pathol* 2008;35:1144-7.
16. Chuh et al. The application of topical tacrolimus in vesicular pemphigoid. *Br J Dermatol* 2004;150:622-3.
17. Ko MJ, Chu CY. Topical tacrolimus therapy for localized bullous pemphigoid. *Br J Dermatol* 2003;149:1079-81.

Articles identified through manual searches:

18. Nazemi-Tabrizi M-J et al. Randomized trial of tacrolimus 0.1% ointment versus triamcinolone acetonide 0.1% paste in the treatment of oral pemphigus vulgaris. *Iran J Dermatol* 2012;15:42-6.

Perioral dermatitis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs Schwarz et al. (2008) Oppel et al. (2007)	R, DB, VC trial (60) R, DB, VC trial (20)	+	80	P P
Level 2 evidence:				
Level 3 evidence: Rodriguez-Martin (2007) Misago et al. (2007)	Case report (1) Case report (1)	+	2	P T + oral minocycline
Other: Lebwohl (2017)	Textbook (NA)	+	NA	P (2 nd -line; Level A)
Lack of effect:				
Evidence of harm:				

DB, double blind; NA: not applicable; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (perioral dermatitis)

Filters: None applied

Total articles retrieved: 16

- 12 excluded at title/abstract filtering stage:
 - 5 non-systematic reviews
 - 3 articles in German
 - 1 case on diagnosis; no TCI treatment
 - 1 article on periocular dermatitis
 - 1 article in Danish
 - 1 case series not specific to perioral dermatitis

Selected full citations:

1. Schwarz T et al. A randomized, double-blind, vehicle-controlled study of 1% pimecrolimus cream in adult patients with perioral dermatitis. JAAD 2008;59:34-40.
2. Oppel T et al. Pimecrolimus cream (1%) efficacy in perioral dermatitis - results of a randomized, double-blind, vehicle-controlled study in 40 patients. JEADV 2007;21:1175-80.
3. Rodriguez-Martin M et al. Treatment of perioral dermatitis with topical pimecrolimus. JAAD 2007;56:529-30.
4. Misago N et al. Childhood granulomatous periorificial dermatitis: lupus miliaris disseminatus faciei in children? JEADV 2005;19:470-3.

Prurigo nodularis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes

Level 1 evidence: RCTs Siepmann et al (2013)	R, DB trial (30)	+	30	P vs TCS
Level 2 evidence: Stander et al (2006)	Open surveillance (11)	+	11	P or T (9/11 had response 20-100%)
Level 3 evidence:				
Other: Qureshi et al. (2018) Lebwohl (2017) Bologna (2018)	Systematic review (30) Textbook (NA) Textbook (NA)	+	30	P ~ TCS P or T (1 st -line; Level A) P or T ("potential benefit")
Lack of effect:				
Evidence of harm:				

DB, double blind; NA: not applicable; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; T: tacrolimus; TCS: topical corticosteroid

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (prurigo nodularis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 7

- 4 excluded at title/abstract filtering stage:
 - 4 non-systematic reviews

Selected full citations:

1. Siepmann D et al. Evaluation of the antipruritic effects of topical pimecrolimus in non-atopic prurigo nodularis: results of a randomized, hydrocortisone-controlled, double-blind phase II trial. Dermatology 2013;227:353-60.

2. Qureshi AA et al. A Systematic Review of Evidence-Based Treatments for Prurigo Nodularis. JAAD 2018 Sep 24 (Epub ahead of print).
3. Stander S et al. Treatment of pruritic diseases with topical calcineurin inhibitors. Ther Clin Risk Manag 2006;2:213-8.

Psoriasis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: RCTs				
Tirado-Sanchez (2012)	RCT (18)	+	321	T vs calcipotriol vs T + calcipotriol
Buder et al (2010)	R, DB trial (14)	+		T +/- TCS
Liao et al. (2007)	R, DB trial (50)	+		T vs calcitriol (FFG PsO)
Kreuter et al. (2006)	R, DB, VC (20)	+		P vs TCS vs calcipotriol vs V ($P < TCS$, $P \sim \text{calcipo}$); intertriginous P (inverse PsO)
Gribetz et al. (2004)	R, DB, VC (28)	+		T (FFG PsO)
Lebwohl et al. (2004)	R, DB, VC (112)	+		T + 6% salicylic acid gel vs 6% salicylic acid gel
Carroll et al. (2004)	RCT (30)	+		P vs calcipotriol vs TCS vs V
Mrowietz et al. (2003)	R, DB, VC (23)	+		P vs TCS vs V (under occlusion)
Mrowietz et al. (1998)	R, DB trial (10)	+		T vs TCS vs calcipotriol vs V (under descaling & occlusion)
Remitz et al. (1999)	R, DB, VC trial (16)	+		
Level 2 evidence:				
Bissonnette et al. (2008)	Open NC trial (12)	+	235	T (male genital PsO)
Vissers et al. (2008)	Open-label, R, SB (12)	+		T gel 0.3% or ointment 0.5% vs calcipotriol
Jacobi et al. (2008)	Open NC (20)	+		P (facial PsO)
Brune et al. (2007)	Open NC (11)	+		T (FFG or inverse PsO, children)
Martin Ezquerra (2006)	Open NC (15)	+		T (with occlusion)
Ortonne et al. (2006)	Open, SB, R (84)	+		T 0.3% vs 0.5% vs calcipotriol
Rallis (2005)	Open NC (10)	+		T (FFG PsO)
Carroll et al. (2005)	Open, R (24)	+		T + 6% salicylic acid gel vs 6% SAG
Freeman et al. (2003)	Open NC (21)	+		T (FFG PsO)
Yamamoto (2000)	Open NC (11)	+		T (Facial PsO)
Rappersberger (1996)	Open NC (15)	+		P (severe recalcitrant PsO)
Level 3 evidence:				
Geller & Kellen (2017)	Case report (1)	+	12	T + TCS (Pt with TNF-induced PsO)
Benoit & Hamm (2013)	Case report (1)	+		T (PsO from a prosthesis/Koebner phenomenon)
Canpolat et al. (2009)	Case report (1)	+		P (infant psoriasis)
Carrascosa et al. (2007)	Case report (1)	+		T + EL (inverse PsO)

Anh et al. (2006) Mansouri (2006) Kroft et al. (2005) Amichai (2004) Clayton et al. (2003)	Case report (1) Case report (1) Case report (1) Case report (1) Case report (1) Case series (4)	+		P (infant) P (child; FFG PsO) T (facial PsO) P (genital PsO) T (facial PsO)
Other:				
Kravvas & Gholam (2018) Albrecht et al. (2011) De Jager et al. (2010) Menter et al. (2009) Kalb et al. (2009) Lebwohl (2017) Bologna (2018)	Systematic review (11) Guideline (NA) Systematic review (20) Guideline (NA) Guideline (NA) Textbook (NA) Textbook (NA)	+	31	T (pediatric PsO; facial & intertriginous) P or T (effective; esp. helpful for FFG areas) T (Grade C for short-term FFG in childhood PsO) P or T (not effective for body PsO; effective for FFG – Level B,II) P or T (for 1 st -line long-term use inverse PsO; Level IB and IIB) P or T (1 st -line for FFG, inverse PsO; Level A) P or T (2 nd -line for FFG)
Lack of effect:				
Hendriks et al. (2013) Rivard et al (2006) Zonneveld (1998)	Systematic review (14) Open NC (6) R, PC trial (24)	0 0 0	44	T adds no benefit when added to TCS T +/- UVA for palmoplantar PsO T no different from PL
Evidence of harm:				
Zirbs et al. (2013) Bronstein et al (2006) Yamamoto (2003)	Case report (1) Case report (1) Case report (1)	- - -	3	P (new onset demodicidosis; pt was on combination tx) T (exacerbation of intercurrent fungal infection) T (deep dermatophytosis; herpes simplex infection)

DB, double blind; EL: excision laser; FFG: face + folds + genitals; NA: not applicable; NC: noncomparative; P: pimecrolimus; PC: placebo controlled; PL: placebo; PsO: psoriasis; pt: patient; R, randomized; RCT, randomized controlled trial; SB: single blind; T: tacrolimus; TCS: topical corticosteroid; TNF: tumor necrosis factor; tx: treatment; UVA: ultraviolet A; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (psoriasis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

- 2) Language: English, French
- 3) Species: Humans

Total articles retrieved: 121

- 79 excluded at title/abstract filtering stage:
 - 3 systemic tacrolimus
 - 4 oral pimecrolimus
 - 19 systemic cyclosporine
 - 2 topical cyclosporine
 - 1 intralesional cyclosporine
 - 1 review refers to TCI in AD (not psoriasis)
 - 8 non-systematic reviews
 - 2 molecular signatures
 - 3 ocular PsO
 - 8 no use of TCI
 - 1 psoriatic cheilitis
 - 1 case of borrelian pseudolymphoma
 - 2 palmoplantar pustular psoriasis
 - 3 generalized pustular PsO
 - 4 nail psoriasis
 - 2 cases verrucous epidermal nevus; no mention of TCI
 - 1 case of psoriasis exclusively of the lips
 - 1 case of osteonecrosis
 - 1 case ustekinumab; prior trial of tacrolimus but no description of response
 - 1 case impetigo herpetiformis
 - 1 consensus conference (not a formal guideline)
 - 1 case granuloma annulare
 - 1 case necrolytic acral erythema
 - 2 studies of alefacept; concomitant TCI was allowed
 - 1 tinea incognito
 - 1 case genital lichen sclerosus
 - 1 case pyririisis rubra pilaris

- 2 cases acrodermatitis continua of Hallopeau/suppurativa
- 1 case GVHD

Selected full citations:

1. Kravvas G, Gharam K. Use of topical therapies for pediatric psoriasis: a systematic review. *Pediatr Dermatol* 2018;35(3):296-302.
2. Geller L, Kellen R. Tumor necrosis factor antagonist-induced psoriasis in a 3-year-old boy with Kawasaki disease. *Dermatol Online J* 2017;23(2). pii: 13030/qt87k9b0x2.
3. Zirbs M et al. Demodicidosis associated with psoriasis therapy – two case reports. *Australas J Dermatol* 2013;54(3):235-6.
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7. Albrecht L et al. Topical psoriasis therapy in the age of biologics: evidence-based treatment recommendations. *JCMS* 2011;15(6):309-21.
8. Buder K et al. Evaluation of methylprednisolone aceponate, tacrolimus and combination thereof in the psoriasis plaque test using sum score, 20-MHz-ultrasonography and optical coherence tomography. *Int J Clin Pharmacol Ther* 2010;48(12):814-20.
9. de Jager ME et al. Efficacy and safety of treatments for childhood psoriasis: a systematic literature review. *JAAD* 2010;62(6):1013-30.
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11. Canpolat F et al. Pimecrolimus 1% cream is effective in the treatment of psoriasis in an infant. *Eur J Dermatol* 2009;19(2):168-9.
12. Kalb RE et al. Treatment of intertriginous psoriasis: from the Medical Board of the National Psoriasis Foundation. *JAAD* 2009;60:120-4.
13. Bissonnette R et al. Efficacy and tolerability of topical tacrolimus ointment for the treatment of male genital psoriasis. *JCMS* 2008;12:230-4.
14. Vissers WHPM et al. Topical treatment of mild to moderate plaque psoriasis with 0.3% tacrolimus gel and 0.5% tacrolimus cream: the effect on SUM score, epidermal proliferation, keratinization, T-cell subsets and HLA-DR expression. *Br J Dermatol* 2008;158(4):705-12.
15. Jacobi A et al. Pimecrolimus 1% cream in the treatment of facial psoriasis: a 16-week open-label study. *Dermatology* 2008;216:133-6.

16. Liao YH et al. Comparison of cutaneous tolerance and efficacy of calcitriol 3 microg g(-1) ointment and tacrolimus 0.3 mg g(-1) ointment in chronic plaque psoriasis involving facial or genitofemoral areas: a double-blind, randomized controlled trial. *Br J Dermatol* 2007;157:1005012.
17. Carrascosa JM et al. Treatment of inverse psoriasis with excimer laser therapy and tacrolimus ointment. *Dermatol Surg* 2007;33:361-3.
18. Brune A et al. Tacrolimus ointment is effective for psoriasis on the face and intertriginous areas in pediatric patients. *Pediatr Dermatol* 2007;24:76-80.
19. Anh SJ et al. A case of infantile psoriasis with pseudoainhum successfully treated with topical pimecrolimus and low-dose narrowband UVB phototherapy. *JEADV* 2006;20:1332-4.
20. Kreuter A et al. 1% pimecrolimus, 0.005% calcipotriol, and 0.1% betamethasone in the treatment of intertriginous psoriasis: a double-blind, randomized controlled study. *Arch Dermatol* 2006;142:1138-43.
21. Rivard J et al. Tacrolimus ointment 0.1% alone and in combination with medium-dose UVA1 in the treatment of palmar or plantar psoriasis. *J Drugs Dermatol* 2006;5:505-10.
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29. Gribetz C et al. Pimecrolimus cream 1% in the treatment of intertriginous psoriasis: a double-blind, randomized study. *JAAD* 2004;51:731-8.
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32. Amichai B. Psoriasis of the glans penis in a child successfully treated with Elidel (pimecrolimus) cream. *JEADV* 2004;18:742-3.
33. Mrowietz U et al. An experimental ointment formulation of pimecrolimus is effective in psoriasis without occlusion. *Acta Derm Venereol* 2003;83:351-3.
34. Clayton TH et al. Topical tacrolimus for facial psoriasis. *Br J Dermatol* 2004;149:419-20.
35. Yamamoto T, Nishioka K. Deep dermatophytosis during topical tacrolimus therapy for psoriasis. *Acta Derm Venereol* 2003;83:291-2.

36. Freeman AK et al. Tacrolimus ointment for the treatment of psoriasis on the face and intertriginous areas. JAAD 2003;48:564-8.
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38. Zonneveld IM et al. Topical tacrolimus is not effective in chronic plaque psoriasis. A pilot study. Arch Dermatol 1998;134:1101-2.
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Rosacea

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: MA Van Zuuren et al. (2015)	Cochrane meta-analysis (105)	+	105	T + PDL > T; P similar to metronidazole
Level 1 evidence: RCTs Koca et al. (2010) Karabulut et al. (2008)	R, open trial (25) R, DB, VC trial (20)	+	45	P vs metronidazole P vs PL (only effect was on erythema)
Level 2 evidence: Kim et al. (2011) Lee et al. (2008) Chu (2007) Bamford et al. (2004)	Open NC trial (30) SB, NC trial (18) Open, NC trial (40) Open, NC trial (24)	+	112	P P P T (only effective on erythema, not lesions)
Level 3 evidence: Qian et al. (2015) Nikolaou et al. (2010) Gul et al. (2008) Sehgal et al. (2008) Cunha & Rossi (2006) Chu (2005) Pabby et al. (2003) Goldman (2001)	Case report (1) Case series (20) Case report (1) Case report (1) Case report (1) Case report (1) Case report (2) Case report (1) Case series (3)	+	30	P + oral thalidomide P (patients with EGFR-related papulopustular eruption) P T + azithromycin P P (steroid-induced rosacea) T + tetracycline T 0.075% ointment
Other:			NA	

Lebwohl (2017) Bologna (2018)	Textbook (NA) Textbook (NA)	++ +/-		P or T 3 rd line P or T (some studies have shown improvement of erythema, but cases of exacerbations; further studies needed)
Lack of effect: Weissenbacher et al (2007)	R, SB, PC trial (25)	0	25	P vs V
Evidence of harm: Chen et al. (2015) El-Heis & Buckley (2015) Hu et al. (2015) Fujiwara et al. (2010) Ogunleye (2008) Yoon et al. (2007) El Sayed et al. (2006) Gorman (2005) Lübbe (2004) Lübbe et al (2003) Bernard et al. (2003) Teraki et al. (2012) Antille t al. (2004)	Case report (1) Case report (1) Case report (1) Case series (3) Case report (1) Case series (16) Case series (6)	- - - - - - - - - - - - - - -	35	T (Kaposi's varicelliform eruption during long-term Tx) P (patient treated for AD) T (granulomatous rosacea recalcitrant to oral tetracyclines) T (rosacea-like eruptions during treatment of facial dermatitis) P (ethanol-induced flushing) P (rosacea-like demodicidosis) P (rosacea eruption in patient with discoid lupus) P (rosaceiform eruption in seborrheic dermatitis patient) T (facial flushing induced by alcohol) P (patient treated for AD) T (patient treated for AD) T or T + TCS T (pts with inflammatory facial dermatoses)

AD: atopic dermatitis; DB: double blind; NA: not applicable; NC: noncomparative; PC: placebo controlled; PDL: pulsed dye laser; PL: placebo; P: pimecrolimus; pt: patient; R, randomized; RCT, randomized controlled trial; SB: single blind; T: tacrolimus; TCS: topical corticosteroid; V: vehicle; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (rosacea)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 37

- 8 excluded at title/abstract filtering stage:
 - 1 on granulomatous periocular eruption
 - 1 on pseudolymphomatous reaction misdiagnosed as rosacea
 - 1 study on atopic dermatitis
 - 1 older version of Cochrane review
 - 2 cyclosporine
 - 2 cases of granulomatous periorificial dermatitis

Selected full citations:

1. Chen QQ et al. Kaposi's varicelliform eruption during long-term treatment of rosacea with 0.03% tacrolimus ointment. *Chin Med J (Engl)* 2015;129(20):2833-4.
2. El-Heis S, Buckley DA. Rosacea-like eruption due to topical pimecrolimus. *Dermatol Online J* 2015;21(5). pii: 13030/qt7kd1048m.
3. Hu L et al. Severe tacrolimus-induced granulomatous rosacea recalcitrant to oral tetracyclines. *J Drugs Dermatol* 2015;14(6):628-30.
4. van Zuuren EJ et al. Interventions for rosacea. *Cochrane Database Syst Rev* 2015;(4):CD003262.
5. Qian G et al. Successful treatment of recalcitrant granulomatous rosacea with oral thalidomide and topical pimecrolimus. *J Dermatol* 2015;42(5):539-40.
6. Kim MB et al. Pimecrolimus 1% cream for the treatment of rosacea. *J Dermatol* 2011;38(12):1135-9.
7. Fujiwara S et al. Rosaceiform dermatitis associated with topical tacrolimus treatment. *JAAD* 2010;62(6):1050-2.
8. Nikolaou V et al. Pimecrolimus cream 1% for the treatment of papulopustular eruption related to epidermal growth factor receptor inhibitors : a case series and a literature review of therapeutic approaches. *Dermatology* 2010;220(3):243-8.
9. Koca R et al. A comparison of metronidazole 1% cream and pimecrolimus 1% cream in the treatment of patients with papulopustular rosacea: a randomized open-label clinical trial. *Clin Exp Derm* 2010;35(3):251-6.
10. Güll U et al. A case of granulomatous rosacea successfully treated with pimecrolimus cream. *J Dermatolog Treat* 2008;19(5):313-5.
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12. Orgunleye T, James WD. Ethanol-induced flushing with topical pimecrolimus use. *Dermatitis* 2008;19(2):E1-2.
13. Lee DH et al. Pimecrolimus 1% cream for the treatment of steroid-induced rosacea: an 8-week split-face clinical trial. *Br J Dermatol* 2008;158(5):1069-76.

14. Karabulut AA et al. A randomized, single-blind, placebo-controlled, split-face study with pimecrolimus cream 1% for papulopustular rosacea. *JEADV* 2008;22(6):729-34.
15. Yoon TY et al. Pimecrolimus-induced rosacea-like demodicidosis. *Int J Dermatol* 2007;46(10):1103-5.
16. Weissenbacher S et al. Pimecrolimus cream 1% for papulopustular rosacea: a randomized vehicle-controlled double-blind trial. *Br J Dermatol* 2007;156(4):728-32.
17. Chu CY. An open-label pilot study to evaluate the safety and efficacy of topically applied pimecrolimus cream for the treatment of steroid-induced rosacea-like eruption. *JEADV* 2007;21(4):484-90.
18. Cunha PR, Rossi AB. Pimecrolimus cream 1% is effective in a case of granulomatous rosacea. *Acta Derm Venereol* 2006;86(1):71-2.
19. El Sayed F et al. Rosaceiform eruption to pimecrolimus. *JAAD* 2006;54(3):548-50.
20. Gorman CR, White SW. Rosaceiform dermatitis as a complication of treatment of facial seborrheic dermatitis with 1% pimecrolimus cream. *Arch Dermatol* 2005;141(9):1168.
21. Chu CY. The use of 1% pimecrolimus cream for the treatment of steroid-induced rosacea. *Br J Dermatol* 2005;152(2):396-9.
22. Lübbe J, Milingou M. Images in clinical medicine. Tacrolimus ointment, alcohol, and facial flushing. *N Engl J Med* 2004;351(26):2740.
23. Bamford JT et al. Tacrolimus effect on rosacea. *JAAD* 2004;50(1):107-8.
24. Pabby A et al. Combination therapy of tetracycline and tacrolimus resulting in rapid resolution of steroid-induced periocular rosacea. *Cutis* 2003;72(2):141-2.
25. Lübbe J et al. Rosaceiform dermatitis with follicular Demodex after treatment of facial atopic dermatitis with 1% pimecrolimus cream. *Dermatology* 2003;207(2):204-5.
26. Bernard LA et al. A rosacea-like granulomatous eruption in a patient using tacrolimus ointment for atopic dermatitis. *Arch Dermatol* 2003;139(2):229-31.
27. Goldman D. Tacrolimus ointment for the treatment of steroid-induced rosacea: a preliminary report. *JAAD* 2001;44(6):995-8.
28. Teraki Y et al. Tacrolimus-induced rosacea-like dermatitis: a clinical analysis of 16 cases associated with tacrolimus ointment application. *Dermatology* 2012;224(4):309-14.
29. Antille C et al. Induction of rosaceiform dermatitis during treatment of facial inflammatory dermatoses with tacrolimus ointment. *Arch Dermatol* 2004;140(4):457-60.

Seborrheic dermatitis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: MA Kastarinen et al. (2014)	Cochrane MA (175)	+	175	P or T comparable to TCS
Level 1 evidence: RCTs Zhao et al. (2018) Goldust et al. (2013) Kim et al. (2013) Papp et al. (2012) Cicek et al. (2009) Shin et al. (2009) Koc et al. (2009) Warshaw et al. (2007) Firooz et al. (2006) Rigopoulos et al. (2004)	RCT (30) RCT (30) R, DB, VC trial (87) SB, RCT (16) RCT (21) RCT (27) Open RCT (23) R, DB, VC trial (47) R, SB trial (20) R, open trial (11)	+	312	P bid then moisturizer vs P bid then qd vs P bid T vs sertaconazole T 2x/w vs T 1x/w vs V T vs TCS (face) P vs TCS vs metronidazole T vs TCS vs zinc pyrithione shampoo P vs ketoconazole P vs V (face) P vs TCS (face) P vs TCS
Level 2 evidence: Ozden et al. (2010) Tatlican et al. (2009) Kim et al. (2007) Rallis et al. (2004) Meshkinpour et al. (2003) Braza et al. (2003) De Moraes et al. (2007) Tatlican et al. (2010) High & Pandya (2006)	Open NC trial (16) Open NC trial (52) Open NC trial (20) Open NC trial (19) Open NC trial (18) Open NC trial (16) Open NC trial (21) Open NC trial (45) Open pilot trial (5)	+	212	P (face) P P (face) P T T P (Face) P (re-treatment after relapse) P
Level 3 evidence: Cunha (2006) Brownell et al. (2003) Crutchfield (2002)	Case series (2) Case report (1) Case report (1)	+	4	P (face; refractory to TCS) P P
Other: Gupta & Versteeg (2017) Hald et al. (2015) Ang-Tiu et al. (2012) Lebwohl (2017) Bologna (2018)	Systematic review (NA) Guideline (NA) Systematic review (106) Textbook (NA) Textbook (NA)	+	106	P or T consistently effective across RCTs P or T (evidence/strength of recommendation: A I-ii for both) P (comparable efficacy as TCS and antimycotics) P or T (2 nd line, level A) P or T (2 nd line)

Lack of effect:				
Evidence of harm:				
Ogunleye (2008)	Case report (1)	-	3	P (ethanol-induced flushing)
Yoon et al. (2007)	Case report (1)	-		P (rosacea-like demodicidosis)
Gorman (2005)	Case report (1)	-		P (rosaceiform dermatitis)

DB, double blind; NA: not applicable; NC: noncomparative; PL: placebo; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SB: single blind; T: tacrolimus; TCS: topical corticosteroid; V: vehicle; VC: vehicle controlled

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (seborrheic dermatitis OR seborrheic eczema OR dandruff OR cradle cap)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 34

- 6 excluded at title/abstract filtering stage:
 - 3 non-systematic reviews
 - 1 meta-analysis on topical antifungals
 - 1 paper reported on the same study in a different journal (Goldust)
 - 1 on GVHD

Selected full citations:

1. Zhao J et al. Comparison of different regimens of pimecrolimus 1% cream in the treatment of facial seborrheic dermatitis. *J Cosmet Dermatol* 2018;17(1):90-94.
2. Gupta AK, Versteeg SG. Topical treatment of facial seborrheic dermatitis: A systematic review. *Am J Clin Dermatol* 2017;18(2):193-213.
3. Kastarinen H et al. Topical anti-inflammatory agents for seborrheic dermatitis of the face or scalp. *Cochrane Database Syst Rev* 2014;(5):CD009446.

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13. Koc E et al. An open, randomized, prospective, comparative study of topical pimecrolimus 1% cream and topical ketoconazole 2% cream in the treatment of seborrheic dermatitis. *J Dermatolog Treat* 2009;20(1):4-9.
14. Orgunleye T, James WD. Ethanol-induced flushing with topical pimecrolimus use. *Dermatitis* 2008;19(2):E1-2.
15. Kim B-S et al. Treatment of facial seborrheic dermatitis with pimecrolimus cream 1%: an open-label clinical study in Korean patients. *J Korean Med Sci* 2007;22:868-72.
16. Yoon TY et al. Pimecrolimus-induced rosacea-like demodicidosis. *Int J Dermatol* 2007;46(10):1103-5.
17. Warshaw EM et al. Results of a randomized, double-blind, vehicle-controlled efficacy trial of pimecrolimus cream 1% for the treatment of moderate to severe facial seborrheic dermatitis. *JAAD* 2007;57(2):257-64.
18. Firooz A et al. Pimecrolimus cream, 1%, vs hydrocortisone acetate cream, 1%, in the treatment of facial seborrheic dermatitis: a randomized, investigator-blind, clinical trial. *Arch Dermatol* 2006;142(8):1066-7.
19. Cunha PR. Pimecrolimus cream 1% is effective in seborrheic dermatitis refractory to treatment with topical corticosteroids. *Acta Derm Venerol* 2006;86(1):69-70.
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Vitiligo

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: MA				
Li R et al. (2017)	Meta-analysis (146)	+	702	P or T combined with NB-UVB
Bae et al. (2016)	Meta-analysis (99)	+		P or T combined with 308-nm EL
Dang YP et al. (2016)	Meta-analysis (337)	+		P or T; mono- and combo (+phototherapy)
Whitton et al. (2015)	Meta-analysis (120)	+		P or T; mono- and combo (+ NB-UVB, 308-nm EL)
Level 1 evidence: RCTs			627	
Cavalie et al. (2015)	R, DB, PC trial (19)	+		T; maintenance (prevention of depigmentation)
Baldo et al (2014)	RCT (24)	+		T vs. NB-UVB
Kathuria et al. (2012)	RCT (19)	-		T vs. TCS
Nistico et al. (2012)	Open-label RCT (20)	+		T + 208-nm EL + oral vitamin E vs. EL + oral vit E vs. oral vit E
Nordal et al. (2011)	R, DB trial (40)	+		T + NB-UVB vs. NB-UVB
Ho et al. (2011)	RCT (31)	+		T vs. TCS vs. PL
Majid (2010)	Single-blind RCT (80)	+		T + NB-UVB vs. NB-UVB
Kose et al. (2010)	Open-label RCT (25)	+/-		P vs. TCS (P only effective for face; not for other body locations)

Klahan et al. (2009)	Single-blind RCT (15)	+		T + NB-UVB vs. NB-UVB
Hui-Lan et al. (2009)	Single-blind RCT (49)	+		P + 308-nm EL
Farajzadeh et al. (2009)	R, PC trial (65)	+		P vs P + microdermabrasion vs. PL
Stinco et al. (2009)	Open-label RCT (31)	+		P vs T vs NB-UVB
Lubaki et al. (2010)	R, DB, PC trial (40)	+		2 trials : T vs PL (R, DB, RCT) and P (nonrandomized trial)
Radakovic et al. (2009)	Single-blind RCT (17)	+		T qd vs bid (best response in facial region)
Eryilmaz et al. (2009)	DB, RCT (16)	+		P vs TCS
Hartmann et al. (2008)	R, PC, DB trial (30)	+		T vs PL
Esfandiarpour et al. (2009)	R, DB, PC trial (25)	+/-		P + NB-UVB vs PL + NB-UVB (positive for face only)
Dawid et al. (2006)	R, DB, PC trial (20)	+/-		P vs vehicle (only effective for face)
Mehrabi & Pandya (2006)	R, DB, PC trial (9)	+		T + NB-UVB vs PL + NB-UVB
Passeron et al. (2004)	RCT (14)	+		T + 308-nm EL vs EL alone
Kawalek et al. (2004)	DB, PC trial (8)	+		T + EL vs PL + EL
Lepe et al. (2003)	R, DB trial (20)	+		T vs TCS
Level 2 evidence:			801	
Dayal et al. (2016)	Open-label trial (20)	+		T + NB-UVB vs NB-UVB
Bapur et al. (2016)	Retrospective study (29)	+		T + EL vs TCS + EL vs EL
Shrestha et al. (2014)	Open-label trial (50)	+		T + TCS vs. TCS + topical placental gel extract
Du et al. (2013)	Open-label extension (34)	+		T or T + TCS
Satyanarayan et al. (2013)	Open-label trial (25)	+		T + NB-UVB vs NB-UVB
Juan et al. (2011)	Open-label trial (36)	+		T vs TCS
Udompataikul et al. (2011)	Open NC trial (42)	+		T
Lo et al. (2010)	Open NC trial (61)	+		T (face and neck only)
Sendur et al. (2006)	Open NC trial (23)	+		P
Boone et al. (2007)	Open pilot study (26)	+		P (head and neck only)
Kanwar et al. (2004)	Open NC trial (25)	+		T
Grimes et al. (2004)	Open NC trial (19)	+		T
Silpa-Archa et al. (2016)	Open pilot study (20)	+		T vs TCS
Park et al. (2016)	Retrospective CR (176)	+		T + EL vs T vs EL
Matin et al. (2014)	Retrospective CR (75)	+		T + EL vs EL
Fai et al. (2007)	Open NC trial (110)	+		T + NB-UVB
Rokni et al. (2017)	Open NC trial (30)	+		T 1% formulation
Level 3 evidence:			43	
Bayer & Chiu. (2017)	Case report (1)	+		P + TCS
Lonowski et al. (2016)	Case report (1)	+		P
Byun et al. (2015)	Case report (1)	+		T + He-Ne laser
Kim & Lee (2013)	Case report (1)	+		T + NB-UVB
Mattox et al. (2013)	Case report (1)	+		T + NB-UVB

Pagliarello & Paradis (2012)	Case report (1)	+		T
Tamler et al. (2011)	Case series (10)	+		T
Lee et al. (2010)	Case series (2)	+		T + TCS
Lan et al. (2009)	Case report (1)	+		T + He-Ne laser
Bila et al. (2009)	Case report (1)	+		T + calcipotriol
Hartmann et al. (2008)	Case series (2)	+		T or P under occlusion
Souza Leite et al. (2007)	Case report (1)	+		P
Mayoral et al. (2003)	Case series (3)	+		P
Travis et al. (2003)	Case report (1)	+		T
Smith et al. (2002)	Case series (15)	+		T
Tanghetti (2003)				
Other:				
de Menezes et al. (2017)	Systematic review (176)	+		P or T; mono- and combo (+ excision laser, microdermabrasion)
Sisti et al. (2016)	Pooled analysis (709)	+		T monotherapy
Gawkrodger et al. (2010)	Guideline (NA)			P or T
Gawkrodger et al. (2008)	Guideline (NA)			P or T
Lebwohl (2017)	Textbook (NA)			P or T; mono- or combined with NB-UVB (1 st -line, level A)
Bologna (2018)	Textbook (NA)			P or T; mono- or combined with NB-UVB or EL; rotation with TCS
Evidence of no effect				
Ostovari et al. (2006)	Open label pilot study (9)	0 (T alone)	9	T vs T + NB-UVB
Evidence of harm				
Gargovich et al.(2016)	Case report (1)	-		T (hereditary Christ-Siemens-Touraine syndrome)
Li et al. (2009)	Case report (1)	-		P (facial acne)
Mikkhail et al. (2008)	Case report (1)	-		T (enlargement of malignant melanoma)
De & Kanwar (2008)	Case report (1)	-		T (hyperpigmentation)
Bakos & Bakos (2007)	Case report (1)	-		T (focal acne)
Narang et al. (2006)	Case report (1)	-		T (verruca vulgaris)
Ahn et al. (2005)	Case report (1)	-		T (molluscum contagiosum infection)
Prats et al. (2005)	Case report (1)	-		T (focal hypertrichosis)

CR: chart review; DB, double blind; EL: excision laser; He-Ne: helium-neon; MDA: microdermabrasion; NA: not applicable; NB-UVB: narrow band ultraviolet B; NC: noncomparative; PC, placebo controlled; PL: placebo; P: pimecrolimus; R, randomized; RCT, randomized controlled trial; SB: single blind; T: tacrolimus; TCS: topical corticosteroid
+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (vitiligo)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 73

- 9 excluded at title/abstract filtering stage:
 - 2 reports in non-target population
 - 4 non-systematic reviews
 - 1 continuing medical education article
 - 1 *in vivo* induction model
 - 1 systematic review with no data on TCIs

Selected full citations:

1. Bae JM et al. The efficacy of 308-nm excimer laser/light (EL) and topical agent combination therapy versus EL monotherapy for vitiligo: A systematic review and meta-analysis of randomized controlled trials (RCTs). *J Am Acad Dermatol* 2016;74(5):907-915.
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3. Bapur Erduran F, Adisen E. Comparison of the efficacy of 308-nm excimer lamp monotherapy with topical tacrolimus or clobetasol 17-propionate combination therapies in localized vitiligo. *Photodermatol Photoimmunol Photomed* 2016;32(5-6):247-253.
4. Bayer ML, Chiu YE. Successful treatment of vitiligo associated with Vogt-Koyanagi-Harada disease. *Pediatr Dermatol* 2017;34(2):204-205.
5. Bila DB et al. Two therapeutic challenges: facial vitiligo successfully treated with 1% pimecrolimus cream and 0.005% calcipotriol cream. *J Eur Acad Dermatol Venereol* 2009;23(1):72-73.
6. Boone B et al. Topical pimecrolimus in the treatment of vitiligo. *Eur J Dermatol* 2007;17(1):55-61.
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11. Dayal S et al. Treatment of childhood vitiligo using tacrolimus ointment with narrowband ultraviolet B phototherapy. *Pediatr Dermatol* 2016;33(6):646-651.
12. de Menezes AF et al. Pharmacologic treatment of vitiligo in children and adolescents : A systematic review. *Pediatr Dermatol* 2017;34(1):13-24.
13. Du J et al. Long-term efficacy and safety of tacrolimus ointment in the treatment of vitiligo. *J Dermatol* 2013;40(11):935-936.
14. Eryilmaz A et al. Pimecrolimus: a new choice in the treatment of vitiligo? *J Eur Acad Dermatol Venereol* 2009;23(11):1347-1348.
15. Farajzadeh S et al. The efficacy of pimecrolimus 1% cream combined with microdermabrasion in the treatment of nonsegmental childhood vitiligo: a randomized placebo-controlled study. *Pediatr Dermatol* 2009;26(3):286-291.
16. Gawkroger DJ et al. Vitiligo: concise evidence-based guidelines on diagnosis and management. *Postgrad Med J* 2010;86(1018):466-471.
17. Gawkroger DJ et al. Guideline for the diagnosis and management of vitiligo. *Br J Dermatol* 2008;159(5):1051-1076.
18. Grimes PE et al. Topical tacrolimus therapy for vitiligo: therapeutic responses and skin messenger RNA expression of proinflammatory cytokines. *J Am Acad Dermatol* 2004;51(1):52-61.
19. Hartmann A et al. Occlusive treatment enhances efficacy of tacrolimus 0.1% ointment in adult patients with vitiligo: results of a placebo-controlled 12-month prospective study. *Acta Derm Venereol* 2008;88(5):474-479.
20. Hartmann A et al. Repigmentation of pretibial vitiligo with calcineurin inhibitors under occlusion. *J Dtsch Dermatol Ges* 2008;6(5):383-385.
21. Ho N et al. A double-blind, randomized, placebo-controlled trial of topical tacrolimus 0·1% vs. clobetasol propionate 0·05% in childhood vitiligo. *Br J Dermatol* 2011;165(3):626-632.
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24. Kanwar AJ et al. Topical tacrolimus for treatment of childhood vitiligo in Asians. *Clin Exp Dermatol* 2004;29(6):589-592.
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26. Kawalek AZ et al. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: a pilot study. *Dermatol Surg* 2004;30(2 Pt 1):130-135.

27. Kim CR, Lee DY. Combination of narrow-band ultraviolet B and topical tacrolimus is effective for segmental vitiligo. *Int J Dermatol* 2013;52(10):1279-1281.
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37. Majid I. Does topical tacrolimus ointment enhance the efficacy of narrowband ultraviolet B therapy in vitiligo? A left-right comparison study. *Photodermat Photoimmunol Photomed* 2010;26(5):230-234.
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39. Mayoral FA et al. Repigmentation of vitiligo with pimecrolimus cream: a case report. *Dermatology* 2003;207(3):322-323.
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45. Radakovic S et al. Response of vitiligo to once- vs. twice-daily topical tacrolimus: a controlled prospective, randomized, observer-blinded trial. *J Eur Acad Dermatol Venereol* 2009;23(8):951-953.
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58. Li JC, Xu AE. Facial acne during topical pimecrolimus therapy for vitiligo. *Clin Exp Dermatol* 2009;34(7):489-90.
59. Mikhail M et al. Rapid enlargement of a malignant melanoma in a child with vitiligo vulgaris after application of topical tacrolimus. *Arch Dermatol* 2008;144(4):560-561.

60. De D, Kanwar AJ. Tacrolimus-induced hyperpigmentation in a patch of vitiligo. *Skinmed* 2008;7(2):93-94.
61. Bakos L, Bakos RM. Focal acne during topical tacrolimus therapy for vitiligo. *Arch Dermatol* 2007;143(9):1223-1224.
62. Narang T et al. Verruca vulgaris following treatment with tacrolimus ointment. *Dermatology* 2006;213(3):254-255.
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64. Prats Caelles I et al. Focal hypertrichosis during topical tacrolimus therapy for childhood vitiligo. *Pediatr Dermatol* 2005;22(1):86-87.

Articles identified through manual searches:

65. Ostovari N et al. Lack of efficacy of tacrolimus in the treatment of vitiligo in the absence of UV-B exposure. *Arch Dermatol* 2006;142(2):252-3.
66. Silpa-Archa N et al. Comparison of the efficacy and safety of 0.1% tacrolimus ointment and 0.1% mometasone furoate cream for adult vitiligo: A single-blinded pilot study. *Dermatologica Sinica* 2016;34(4):177-9.
67. Park OJ et al. A combination of excimer laser treatment and topical tacrolimus is more effective in treating vitiligo than either therapy alone for the initial 6 months, but not thereafter. *Clin Exp Dermatol* 2016;41(3):236-41.
68. Rokni GR et al. Effectiveness and safety of topical tacrolimus in treatment of vitiligo. *J Adv Pharma Technol Res* 2017;8(1):29-33.
69. Tanghetti EA. Tacrolimus ointment 0.1% produces repigmentation in patients with vitiligo: results of a prospective patient series. *Cutis* 2003;71(2):158-62.
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Disorders with Level 2 evidence and lower

Alopecia Areata

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence				
Level 2 evidence Ucak H et al. (2012)	Case control trial: P (50) vs PL (20) vs control (30)		50	
Level 3 evidence				
Evidence of harm				
Lack of effect Thiers (2000) Price et al. (2005) Rigopoulos et al. (2007) Hunter N et al. (2011)	Case report (1) Open label (11) Pilot study (12) Case control (25) vs. PL (25)	0 0 0 0	49	T T P T

P, pimecrolimus; PL, placebo; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (alopecia areata)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 11

- 6 excluded at title/abstract filtering stage:

- 1 report in non-target population
- 1 systematic review with no data on TCIs
- 1 non-systematic review
- 1 oral TAC
- 2 no report of TCI use

Selected full citations:

1. Theirs BH. Topical Tacrolimus: Treatment Failure in a Patient with Alopecia Areata. Arch Dermatol 2000;136(1):124.
2. Price VH et al. Topical Tacrolimus in Alopecia Areata. J Am Acad Dermatol 2005;52(1):138-139.
3. Rigopoulos D et al. Lack of Response of Alopecia Aerata to Pimecrolimus cream. Clin Exp Dermatol 2007; 32(4):455-456.
4. Hunter N et al. Diphencyprone and Topical Tacrolimus as Two Topical Immunotherapeutic Modalities. Are they Effective in the Treatment of Alopecia Areata among Egyptian Patients? A study Using CD4, CD8 and MHC II as Markers. J Dermatol Treat 2011; 22: 2-10.
5. Ucak H et al. The Comparison of Treatment with Clobetasol Propionate 0.05% and Topical Pimecrolimus 1% Treatment in the Treatment of Alopecia Areata. J Dermatolog Treat 2012;23(6):410-420.

Atopic ocular/periocular disease (eyelid eczema)

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				1
Level 2 evidence: Nivenius et al. (2007)	Case control trial (25)		25	T
Level 3 evidence: Sakarya & Sakarya (2012) Myyazaki et al. (2008) Joseph et al. (2005) Rikkers et al (2003)	Case report (1) Case series (10) Case series (3) Case series (5)	+	19	T T T T
Evidence of harm Moncourier et al. (2017) Joseph et al. (2005)	Case report (1) Case report (1)	-	2	T T

Lack of effect				
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T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (atopic ocular disease OR atopic periocular disease)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 14

- 8 excluded at title/abstract filtering stage:
 - 1 animal study
 - 5 ciclosporin
 - 1 non-target population
 - 1 systemic tacrolimus

Selected full citations:

1. Sakarya Y, Sakarya R. Treatment of Refractory Atopic Blepharoconjunctivitis with Topical Tacrolimus 0.03% Dermatologic Ointment. *J Ocul Pharmacol Ther* 2012; 28(1): 94-96.
2. Miyazaki D et al. Therapeutic Effects of Tacrolimus Ointment for Refractory Ocular Surface Inflammatory Diseases. *Ophthalmol* 2008; 115(6): 988-992.
3. Nivenius E et al. Tacrolimus Ointment vs. Steroid Ointment for Eyelid Dermatitis in Patients with Atopic Keratoconjunctivitis. *Eye (Lond)* 2007; 21(7): 968-975.
4. Joesph MA et al. Topical Tacrolimus Ointment for Treatment of Refractory Anterior Segment Inflammatory Disorders. *Cornea* 2005; 24(4):417-420.
5. Rikkers SM et al. Topical Tacrolimus Treatment of Atopic Eyelid Disease. *Am J Ophthalmol.* 2003;135(3):297-302.
6. Moncourier M et al. Granulomatous Periocular Eruption. *Ann Dermatol Venereol* 2017; 144(6-7):430-433.

Chronic actinic dermatitis, recalcitrant and erythrodermic

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Uetsu et al. (2002)	Open-label trial (6)		6	T
Level 3 evidence : Alquier-Bouffard et al. (2007) Gröne et al. (2006) Baldo et al. (2005) Larangeira de Almeida (2005) Schuster et al. (2004) Evans et al. (2004) Ogawa et al. (2003) Suga et al. (2002)	Case series (2) Case report (1) Case report (1) Case report (1) Case report (1) Case report (1) Case report (1) Case report (1)		9	T T T P T T T T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: [(topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI)] and [(Chronic actinic dermatitis OR recalcitrant chronic actinic dermatitis OR erythrodermic chronic actinic dermatitis)]

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 16

- 7 excluded at title/abstract filtering stage:

- 6 non-target disorder
- 1 article not available

Selected full citations:

1. Alquier-Bouffard A et al. Chronic Actinic Dermatitis: Treatment with Topical Tacrolimus (Two Cases)]. Ann Dermatol Venereol 2007;134(6-7):555-8.
2. Gröne D et al. Successful Treatment of Nodular Actinic Reticuloid with Tacrolimus Ointment. Dermatology 2006;212(4):377-80
3. Baldo A et al. A Case of Chronic Actinic Dermatitis Treated with Topical Tacrolimus. J Dermatolog Treat 2005;16(4):245-248.
4. Larangeira de Almeida H Jr. Successful Treatment of Chronic Actinic Dermatitis with Topical Pimecrolimus. Int J Dermatol 2005;44(4):343-4.
5. Schuster C et al. Successful Treatment of Recalcitrant Chronic Actinic Dermatitis with Tacrolimus. Dermatology 2004;209(4):325-328.
6. Evans AV et al. Erythrodermic Chronic Actinic Dermatitis Responding Only to Topical Tacrolimus. Photodermatol Photoimmunol Photomed 2004;20(1):59-61.
7. Ogawa Y et al. The Successful Use of Topical Tacrolimus Treatment for a Chronic Actinic Dermatitis Patient with Complications of Idiopathic Leukopenia. J Dermatol 2003;30(11):805-9.
8. Uetsu N et al. Treatment of Chronic Actinic Dermatitis with Tacrolimus Ointment. J Am Acad Dermatol 2002;47(6):881-4
9. Suga Y et al. Topical Tacrolimus for Chronic Actinic Dermatitis. J Am Acad Dermatol 2002;46(2):321-3.

Chronic relapsing dyshidrotic palmoplantar eczema

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Schnopp et al. (2002)	Case control trial (16)	+	16	T
Level 3 evidence:				
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: [(topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and [(Chronic relapsing dyshidrotic palmoplantar eczema)]

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 1

Selected full citations:

1. Schnopp C et al. Topical Tacrolimus (FK506) and Mometasone Furoate in Treatment of Dyshidrotic Palmar Eczema: A Randomized, Observer-Blinded Trial. J Am Acad Dermatol 2002; 46(1):73-77.

Dermatomyositis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Hollar & Jorizzo. (2004)	Open pilot trial (6)		6	T
Level 3 evidence: Black & Marshman. (2011) Peyrot et al (2006) Lampropoulos & D' Cruz (2005) Ueda et al (2003) Yoshimasu et al (2002)	Case report (1) Case series (3) Case report (1) Case report (1) Case series (2)	+	8	T T T T T (only 2 of 3 cases were positive)
Evidence of harm				
Lack of effect			1	

Yoshimasu et al. (2002)	Case series (1)	0		T
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T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Dermatomyositis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 7

- 1 excluded at title/abstract filtering stage:
 - 1 due to no exposure to TCI

Selected full citations:

1. Black M, Marshman G. Dermatomyositis and Pemphigus Vulgaris: Association or Coincidence? *Australas J Dermatol* 2011;52(2):11-14.
2. Peyrot I et al. [Topical Tacrolimus and Resistant Skin Lesions of Dermatomyositis. *Rev Med Interne* 2006;27(10):730-735
3. Lampropoulos CE, D'Cruz DP. Topical Tacrolimus Treatment in a Patient with Dermatomyositis. *Ann Rheum Dis* 2005;64(9):1376-7
4. Hollar CB, Jorizzo JL. Topical Tacrolimus 0.1% Ointment for Refractory Skin Disease in Dermatomyositis: a Pilot Study. *J Dermatolog Treat* 2004;15(1):35-9
5. Ueda M et al. Successful Treatment of Amyopathic Dermatomyositis with Topical Tacrolimus. *Br J Dermatol* 2003;148(3):595-6.
6. Yoshimasu T et al. Topical FK506 (tacrolimus) Therapy for Facial Erythematous Lesions of Cutaneous Lupus Erythematosus and Dermatomyositis. *Eur J Dermatol* 2002;12(1):50-2.

Dyshidrotic palmar eczema

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Schnopp et al (2002)	R, SB, intra-individual comparison	+	16	T
Level 3 evidence: Schurmeyer-Horst (2007)	Case report (1)	+	1	P
Evidence of harm				
Lack of effect				

P, pimecrolimus; R, randomized; SB, single blind; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Dyshidrotic palmar eczema)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 2

Selected full citations:

1. Schnopp C et al. Topical Tacrolimus (FK506) and Mometasone Furoate in Treatment of Dyshidrotic Palmar Eczema: a Randomized, Observer-blinded Trial. J Am Acad Dermatol 2002;46(1):73-77.

2. Schurmeyer-Horst F et al. Long-term efficacy of occlusive therapy with topical pimecrolimus in severe dyshidrosiform hand and foot eczema. Dermatology 2007;214(1):99-100.

Genital Lichen Planus

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Bradford (2013)	Retrospective CR (45)	+	45	T
Level 3 evidence : Byrd et al (2004) Lonsdale-Eccles (2005) Helgesen et al (2010) Jang & Fischer (2008) Kortekangas-Savolainen (2007) Amstey (2003) Lotery & Galask (2003) Watsky (2003) Kirtschig et al (2002)	Case series (15) Case series (9) Case series (9) Case series (4) Case series (5) Case report (1) Case series (3) Case report (1) Case report (1)	+	48	T P T T + MTX + TCS T + MTX T T T T
Evidence of harm Lonsdale-Eccles (2005) Lonsdale-Eccles (2004)	Case series (2) Case report (1)	-	3	P T
Lack of effect Byrd et al (2004) Helgesen et al (2010)	Case report (1) Case series (13)	0 0	14	T T

CR, chart review; MTX, methotrexate; P, pimecrolimus; T, tacrolimus; TCS, topical corticosteroid

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (genital lichen planus disease)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 10

5 excluded at title/abstract filtering stage:

- 5 other disease

Selected full citations:

1. Lim SJ, Love EW. Steroid Free pimecrolimus (Elidel) for monotherapy of lichen planus. *J Drugs Dermatol* 2004; 3(5):563-4.
2. Byrd JA et al. Recalcitrant symptomatic vulvar lichen planus: response to topical tacrolimus. *Arch Dermatol*. 2004 Jun;140(6):715-20.
3. Lonsdale-Eccles AA, Velangi S. Topical pimecrolimus in the treatment of genital lichen planus: a prospective case series. *Br J Dermatol* 2005;153(2):390-4.
4. Helgesen AL et al. Vaginal involvement in genital erosive lichen planus. *Acta Obstet Gynecol Scand* 2010;89(7):966-70.
5. Bradford J, Fischer G. Management of vulvovaginal lichen planus: a new approach. *J Low Genit Tract Dis* 2013;17(1):28-32.

Identified through manual search:

6. Jang N, Fischer G. Treatment of erosive vulvovaginal lichen planus with methotrexate. *Australas J Dermatol* 2008; 49(4):216-219.
7. Kortekangas-Savolainen O, Kiilholma P. Vulvovaginal erosive and stenosing lichen planus surgical dilation and methotrexate. *Acta Obstet Gynecol Scand* 2007;86(3):339-343.
8. Amstey MS. Erosive lichen planus of the vulva and vagina. *Obstet Gynecol* 2003;102(3):645.
9. Lotery HE, Galask RP. Erosive lichen planus of the vulva and vagina. *Obest Gynceol* 2003;101(5):1121-1125.
10. Watsky KL. Erosive perianal lichen planus responsive to tacrolimus. *Int J Dermatol* 2003;42(3):217-218.
11. Kirtschig G et al. Successful treatment of erosive vulvovaginal lichen planus with tacrolimus. *Br J Dermatol* 147(3):625-626.
12. Lonsdale-Eccles et al. Herpes simplex of the vulva evoked by topical tacrolimus treatment. *Clin Exp Dermatol* 2005;30:95-6.

Graft vs. Host disease

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Elad et al (2003)	Open-label (7)	+	7	T
Case reports/series				
Brown et al (2013)	Case report (1)	+	46	T
Zangrilli et al (2010)	Case report (1)	+		P
Bauters et al (2010)	Case report (1)	+		T
Tam et al (2010)	Case report (1)	+		T
Rojas et al (2008)	Case report (1)	+		T
Kunitomi et al (2008)	Case report (1)	+		T
Schlaak et al (2008)	Case report (1)	+		T
Fricain et al (2007)	Case series (3)	+		T
Heinemann et al (2005)	Case report (1)	+		T
Schmook et al (2005)	Case report (1)	+		P
Eckardt et al (2004)	Case series (3)	+		T
Ziemer et al (2004)	Case report (1)	+		P
Sánchez et al (2004)	Case report (1)	+		T
Choi & Nghiem (2001)	Case series (13)	+		T
Ogawa et al (2001)	Case series (2)	+		T
Conrotto et al (2006)	Case report (1)	+		T
Prot-Labarthe et al (2007)	Case report (1)	+		T
Evidence of harm				
Prot-Labarthe et al (2007)	Case report (1)		7	T
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (graft vs. host disease)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 38

- 20 excluded at title/abstract filtering stage:
 - 11 excluded due to no TCI use
 - 1 excluded due to lack of access to full article
 - 6 excluded due to non-target disorder
 - 2 non-consensus guidelines

Selected full citations:

1. Brown RS et al. Topical tacrolimus with custom trays in the treatment of severe oral chronic graft-versus –host disease refractory to a potent topical steroid therapy: a case report. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013;115(4):e26-30.
2. Zangrilli A et al. Treatment of disfiguring chronic graft versus host disease in a child with topical pimecrolimus. *Pediatr Int* 2010; 52(3):e161-163.
3. Bauters T et al. Highly effective treatment with tacrolimus ointment in an adolescent with oral graft-versus-host disease. *Pharm World Sci* 2010; 32(3):350-352.
4. Tam PM et al. Topical 0.03% tacrolimus ointment in the management of ocular surface inflammation in chronic GVHD. *Bone Marrow Transplant* 2010; 45(5):957-958.
5. Rojas AG et al. Graft versus host disease with oral involvement: report of one case. *Rev Med Chil* 2008;136(12):1570-1573.
6. Kunitomi A et al (2008). Successful treatment using tacrolimus ointment for cutaneous graft-versus-host disease. *Int J Hematol* 2008;88(4):465-467.
7. Schlaak M A et al. Oral graft-versus-host disease: successful treatment therapy with extracorporeal photopheresis and topical tacrolimus 2008;22(1):112-113.

8. Prot-Labarthe S et al. Toxic serum levels of tacrolimus after topical administration in an infant with severe cutaneous graft-versus-host disease. *Bone Marrow Transplant* 2007;40(3):295-296.
9. Frician JC et al. Long term efficacy of topical tacrolimus on oral lesions of chronic graft-versus-host disease. *Br J Dermatol* 2007; 156(3): 588-90
10. Conrotto D et al. Dramatic increase of tacrolimus plasma concentration during topical treatment for oral graft-versus-host disease. *Transplantation* 2006; 82(8): 1113-1115.
11. Heinemann C et al. Topical tacrolimus in severe chronic graft-versus-host disease. *Acta Derm Venerol* 2005;85(4):370-371.
12. Schmook T et al. Treatment of cutaneous chronic graft-versus-host disease with topical pimecrolimus. *Bone Marrow Transplant* 2005;36:87-88.
13. Eckhardt A et al. Severe oral chronic graft-versus-host disease following allogeneic bone marrow transplantation: highly effective treatment with topical tacrolimus. *Oral Oncol* 2004; 40(8):811-814.
14. Ziemer M et al. Treatment of extensive chronic cutaneous graft-versus-host disease in an infant with topical pimecrolimus. *J Am Acad Dermatol* 2004;50(6):946-948.
15. Sánchez AR et al. Successful treatment of oral lichen planus-like chronic graft-versus-host disease with topical tacrolimus: a case report. *J Periodontol* 2004; 75(4):613-619.
16. Elad S et al. Topical tacrolimus—a novel treatment alternative for cutaneous chronic graft-versus-host disease. *Tranpl Int* 2003;16(9):655-670.
17. Choi CJ, Nghiem P. Tacrolimus ointment in the treatment of chronic cutaneous graft-versus-host disease: a case series of 18 patients. *Arch Dermatol* 2001;137(9):1202-1206.
18. Ogawa Y et al. Successful treatment of dry eye in two patients with chronic graft-versus-host disease with systemic administration of FK506 and corticosteroids. *Cornea* 2001;20(4):430-434.

Lichen simplex chronicus

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Goldstein et al (2007)	Open-label trial (12)	+	24	P
Level 3 evidence:			13	

Kelekci et al (2008) Aschoff & Wozel (2007)	Case series (12) Case report (1)	+		P T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Lichen simplex chronicus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 5

- 2 excluded at title/abstract filtering stage:
 - 2 due to non-target disorder

Selected full citations:

1. Kelekci HK et al. Pimecrolimus 1% cream for pruritus in postmenopausal diabetic women with vulvar lichen simplex chronicus: a prospective non-controlled case series. *J Dermatolog Treat* 2008;19(5):274-278.
2. Goldstein AT et al. Pimecrolimus cream 1% for treatment of vulvar lichen simplex chronicus: an open-label, preliminary trial. *Gynecol Obstet Invest* 2007;64(4):180-186.
3. Aschoff R, Wozel G. Topical tacrolimus for the treatment of lichen simplex chronicus. *J Dermatolog Treat* 2007;18(2):115-117.

Lichen striatus

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Campanati et al (2008)	Open-label trial (3)		3	T
Level 3 evidence: Suárez-Peña et al (2017) Kim et al (2009) Tejera-Vaquerizo et al (2009) Vukićević et al (2009) Jo et al (2007) Sáez-Rodríguez et al (2006) Kus & Ince (2006) Fujimoto et al (2003)	Case series (3) Case report (1) Case report (1) Case report (1) Case series (2) Case report (1) Case report (1) Case report (1)		11	T T T T T P P T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Lichen striatus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 10

- 1 excluded at title/abstract filtering stage due to non-exposure to TCI

Selected full citations:

1. Suárez- Peñaranda JMI et al. Unusual interface dermatoses distributed along blaschko's lines in adult patients. *Am J Dermatopathol* 2017;39(2):144-149.
2. Kim GW et al. Lichen striatus with nail abnormality successfully treated with tacrolimus ointment. *J Dermatol* 2009;36(11):616-7.
3. Tejera-Vaquerizo A et al. Adult blaschkitis (lichen striatus) successfully treated with topical tacrolimus. *Actas Dermosifiliogr* 2009;100(7):631-2.
4. Vukićević J et al. Unilateral multiple lichen striatus treated with tacrolimus ointment: a case report. *Acta Dermatovenerol Alp Pannonica Adriat* 2009;18(1):35-8.
5. Campanati A et al. Lichen striatus in adults and pimecrolimus: open, off-label clinical study. *Int J Dermatol* 2008;47(7):732-6.
6. Jo JH et al. Early treatment of multiple and spreading lichen striatus with topical tacrolimus. *J Am Acad Dermatol* 2007;57(5):904-5.
7. Sáez-Rodríguez M et al. Lichen striatus in an adult successfully treated with pimecrolimus cream. *J Eur Acad Dermatol Venereol* 2006;20(9):1140-1.
8. Kus S, Ince U. Lichen striatus in an adult patient treated with pimecrolimus. *J Eur Acad Dermatol Venereol* 2006;20(3):360-1.
9. Fujimoto N et al. Facial lichen striatus: successful treatment with tacrolimus ointment. *Br J Dermatol* 2003;148(3):587-90.

Nail psoriasis

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: De Simone et al (2013)	Open-label trial (21)		21	T
Level 3 evidence:				
Evidence of harm				
Lack of effect				

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T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Nail psoriasis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 10

- 9 excluded at title/abstract filtering stage:
 - 5 no exposure to TCIs
 - 2 unable to access full text for review
 - 1 due to non-target disorder
 - 1 review with no data on TCIs

Selected full citations:

1. De Simone C et al. Tacrolimus 0.1% ointment in nail psoriasis: a randomized controlled open-label study. J Eur Acad Dermatol Venereol 2013;27(8):1003-6.

Netherton syndrome

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				

Level 2 evidence: Yan et al (2010)	Open-label trial (3)	+	3	P
Level 3 evidence : Henno et al (2006) Oji et al (2005) Beljan et al (2003) Allen et al (2001)	Case series (2) Case report (1) Case report (1) Case series (3)	+	7	P P T T
Evidence of harm Sun & Linden (2006)	Case report (1)	-	1	T
Lack of effect Sun & Linden (2006)	Case report (1)	0		T

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Netherton syndrome)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

- 2) Language: English, French
- 3) Species: Humans

Total articles retrieved: 7

- 1 excluded at title/abstract filtering stage (unable to retrieve full text for review)

Selected full citations:

1. Yan AC et al. The safety and efficacy of pimecrolimus, 1% cream for the treatment of Netherton syndrome: results from an exploratory study. Arch Dermatol 2010;146(1):57-62.
2. Sun JD, Linden KG. Netherton syndrome: a case report and review of the literature. Int J Dermatol 2006;45(6):693-697.

3. Henno A et al. Improvement of Netherton syndrome associated erythroderma in two adult sisters through use of topical pimecrolimus. Ann Dermatol Venereol 2006;133(1):71-72.
4. Oji V et al. Topical pimecrolimus: a novel therapeutic option for Netherton syndrome. Br J Dermatol 2005;153(5):1067-1068.
5. Beljan G et al. [Comèl-Netherton syndrome with bacterial superinfection]. Hautarzt 2003;54(12):1198-1202.
6. Allen A et al. Significant absorption of topical tacrolimus in 3 patients with Netherton syndrome. Arch Dermatol 2001;137(6):747-750.

Paronychia

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence: Rigopoulos et al (2009)	R, unblinded, PC trial (15)	+	15	T (15) PL (15) Control (15)
Level 3 evidence:				
Evidence of harm				
Lack of effect				

PC, placebo controlled; PL, placebo; R, randomized; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Paronychia)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 2

- 1 excluded at title/abstract filtering stage (due to non-target disorder)

Selected full citations:

1. Rigopoulos D et al. Efficacy and safety of tacrolimus ointment 0.1% vs. betamethasone 17-valerate 0.1% in the treatment of chronic paronychia: an unblinded randomized study. Br J Dermatol 2009;160(4):858-860.

Perianal Crohn's disease

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence: McSharry et al. (2011)	Systematic review (14)	+	14	T (ointment 0.5-1.0 mg/g)
RCTs Hart et al. (2007)	R, PC trial (10)	+/-	10	T (1 mg/g; ulcerating disease; not effective in fistulizing)
Level 2 evidence: Casson et al. (2000) Rice et al. (2013)	Open, NC trial (8) Open, NC trial (12)	+ +	20	T (0.5 mg/g; pediatric perianal and oral Crohn's) T (12 or 20 pts had perianal Crohn's disease)
Level 3 evidence:				
Lack of effect:				
Evidence of harm: Ali & Lyon (2013)	Case report (1)		1	T (nausea, paresthesia, light-headedness; high serum levels)

NC: noncomparative; PC, placebo controlled; R, randomized; RCT, randomized controlled trial; T: tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (chronic pruritus)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 5

- 1 excluded at title/abstract filtering stage:
 - 1 article in other language

Selected full citations:

1. McSharry K et al. Systematic review: the role of tacrolimus in the management of Crohn's disease. *Aliment Pharmacol Ther* 2011;34(11-12):1282-1294.
2. Hart AL et al. Topical tacrolimus in the treatment of perianal Crohn's disease: exploratory randomized controlled trial. *Inflamm Bowel Dis* 2007;13(3):245-253.
3. Casson DH et al. Topical tacrolimus may be effective in the treatment of oral and perianal Crohn's disease. *Gut* 2000;47(3):436-440.
4. Ali FR, Lyon CC. Tacrolimus toxicity following topical treatment of perianal Crohn's disease: an admonitory anecdote. *J Crohns Colitis* 2013;7(12):713.

Articles identified through manual searches:

5. Rice AS et al. Topical tacrolimus 0.1% ointment for treatment of cutaneous Crohn's Disease. *BMC Res Notes* 2013;6:19.

Pyoderma gangrenosum

Citations	Type of evidence (n-value for each)	Results	Total population studied *	Notes
Level 1 evidence:			3	

NA, not applicable; P, pimecrolimus; PG, pyoderma gangrenosum; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Pyoderma gangrenosum)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 44

- 16 excluded at title/abstract filtering stage:
 - 13 no TCI use
 - 1 article in Spanish
 - 1 surgical case studies
 - 1 non-target disorder

Selected full citations:

1. Crouse L et al. Pyoderma gangrenosum in an infant: A case report and review of the literature. *Pediatr Dermatol* 2018;35(5):e257-e261.
2. Turrión-Merino L et al. A case series of 4 patients with peristomal pyoderma gangrenosum: review of risk factors and treatment response. *Actas Dermosifiliogr* 2016;107(3):e13-17.
3. Doren EL, Aya-ay ML. Pyoderma gangrenosum following breast reduction: treatment with topical tacrolimus and steroids. *Anesthet Surg J* 2014;34(3):394-399.
4. Rice SA et al. Topical tacrolimus 0.1% ointment for treatment of cutaneous Crohn's disease. *BMC Res Notes* 2013;6:19
5. Cecchi R et al. Successful treatment of localized pyoderma gangrenosum with topical pimecrolimus. *J Cutan Med Surg* 2012;5:295-297.
6. Larsen CG, Thyssen JP. Pustular penile pyoderma gangrenosum successfully treated with topical tacrolimus ointment. *Acta Derm Venereol* 2012;92(1):104-5

7. Tao W et al. Superficial granulomatous pyoderma accompanied with ulcerative colitis successfully treated with tacrolimus ointment. *J Dermatol* 2011;38(11):1105-1108.
8. Alteiri M et al. Topical tacrolimus for parastomal pyoderma gangrenosum: a report of two cases. *Ostomy Wound Manage* 2010;56(9):56-59.
9. Lucchina S et al. FK-506 ointment: An effective adjuvant therapy to treat a dramatic case of pyoderma gangrenosum of unilateral hand. *Chin J Traumatol* 2009;12(3):181-183.
10. Chandrasekhara PK et al. successful treatment of pyoderma gangrenosum associated with juvenile idiopathic arthritis with a combination of topical tacrolimus and oral prednisolone. *Clin Rheumatol* 2009;28(4):489-490.
11. Contreras-Ruiz J et al. Delayed diagnosis of pyoderma gangrenosum: a case study. *Ostomy Wound Manage* 2008;54(11):32-36.
12. Bellini V et al. successful treatment of severe pyoderma gangrenosum with pimecrolimus cream 1%. *J Eur Acad Dermatol Venereol* 2008;22(1):113-115.
13. Kontos AP et al. An open label study of topical tacrolimus ointment 0.1% under occlusion for the treatment of pyoderma gangrenosum. *Int J Dermatol* 2006;45(11):1383-1385.
14. Roé E et al. A case of vulvar pyoderma gangrenosum associated with collagenous colitis. *Dermatology* 2006;213(3):234-235.
15. Pitarch G et al. Systemic absorption of topical tacrolimus in pyoderma gangrenosum. *Acta Derm Venereol* 2006;86(1):64-65.
16. Lally A et al. Penile pyoderma gangrenosum treated with topical tacrolimus. *Arch Dermatol* 2005;141(9):1175-1176.
17. Chiba T et al. Topical tacrolimus therapy for pyoderma gangrenous. *J Dermatol* 2005;32(3):199-203.
18. Deckers-Kochen JM, Pasmans SG. Successful tacrolimus (FK506) therapy in a child with pyoderma gangrenosum. *Arch Dis Child* 2005; 90(5):531.
19. Vidal D, Almoar A. Successful treatment of periostomal pyoderma gangrenosum using topical tacrolimus. *Br J Dermatol* 2004; 150(2):387-388.
20. Kimble RM et al. Successful topical tacrolimus (FK506) therapy in a child with pyoderma gangrenosum. *J Pediatr Gastroenterol Nutr* 2002;34(5):555-557.
21. Skaehill PA. Tacrolimus in dermatologic disorders. *Ann Pharmacother* 2011;35(5):582-588
22. Petering H et al. Pyoderma gangrenosum: successful topical therapy with tacrolimus (FK506). *Hauzart* 2001;52(1):47-50.
23. Ritcher-Hintz et al. Topical tacrolimus (FK506) is effective in the treatment of pyoderma gangrenosum. *J Am Acad Dermatol* 2000 42(2):304-305.
24. Schuppe HC et al. topical tacrolimus for pyoderma gangrenosum. *Lancet* 1998;351(9105):832.
25. Meissner et al. Pyoderma Gangrenosum, a Rare, but Potentially Fatal Complication in Paediatric Oncology Patients. *Klin Padiatr* 2007;219:296-9.

26. Piccirillo et al. Topical tacrolimus for pyoderma gangrenosum: Another report. *J Dermatol* 2006;3:232.
27. Ghislain P-D et al. Efficacy and systemic absorption of topical tacrolimus used in pyoderma gangrenosum. *Br J Dermatol* 2004;150:1052-3.
28. Jolles et al. Combination oral and topical tacrolimus in therapy-resistant pyoderma gangrenosum. *Br J Dermatol* 1999;140:564-5.

Disorders with Level 3 evidence only

Amyloidosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Castanedo-Cazares JP (2002) Kalkan et al. (2014)	Case report (1) Case report (1)	+ +	2	T T + UVB
Evidence of harm				
Lack of effect				

T, tacrolimus; UVB: ultraviolet B radiation

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (amyloidosis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 2

Selected full citations:

1. Castanedo-Cazares JP et al. Lichen Amyloidosis Improved by 0.1% Topical Tacrolimus. *Dermatol* 2002;205(4):420-421.
2. Kalkan G et al. An Alternative Treatment Model: the Combination Therapy of Narrow Band Ultraviolet B Phototherapy and Tacrolimus Ointment 0.1% in Biphasic Amyloidosis. *J Pak Med Assoc* 2014;64(5):579-82.

Angiolymphoid hyperplasia with eosinophilia

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Youssef et al. (2018) Harada et al. (2017) Nouchi et al. (2015) Chacon & Mercer (2016) Wang & Li (2010) Mashiko et al. (2006)	Case report (1) Case report (1) Case series (2) Case report (1) Case report (1) Case report (1)	++ ++ ++ ++ ++ ++	7	T T T T T T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: [(topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI)] and [(Angiolymphoid hyperplasia with eosinophilia)]

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

- 2) Language: English, French
- 3) Species: Humans

Total articles retrieved: 7

- 1 excluded at title/abstract filtering stage:
 - Non-target disorder

Selected full citations:

1. Youssef A et al. Angiolympoid Hyperplasia with Eosinophilia: A Case Report. *J Med Case Rep* 2018;12(1):89.
2. Harada S et al. Complete Remission of Angiolympoid Hyperplasia with Eosinophilia using Topical Tacrolimus. *Eur J Dermatol* 2017;27(2):194-196.
3. Nouchi A et al. Treatment of Angiolympoid Hyperplasia with Eosinophilia (ALHE) using Topical Tacrolimus: Two Cases. *Ann Dermatol Venereol* 2015;142(5):360-366.
4. Chacon A, Mercer J. Successful management of Angiolympoid Hyperplasia with Eosinophilia in a Split Face Trial of Topical Tacrolimus and Timolol Solution. *G Ital Dermatol Venereol* 2016;151(4):436-40.
5. Wang S, Li W. Angiolympoid Hyperplasia with Eosinophilia Successfully Treated with Tacrolimus Ointment. *J Eur Acad Dermatol Venereol* 2010;24(4):237.
6. Mashiko M et al. A Case of Angiolympoid Hyperplasia with Eosinophilia Successfully Treated with Tacrolimus Ointment. *Br J Dermatol* 2006;154(4):803-4.

Cheilitis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence:			14	

Yamaguchi et al. (2016)	Case report (1)	+		T
Apalla et al. (2015)	Case series (2)	+		T
da Cunha Filho et al. (2014)	Case report (1)	+		P
Yoshimura et al. (2013)	Case report (1)	+		T
Hanami et al. (2011)	Case series (2)	+		T
Choi et al. (2009)	Case series (4)	+		T (n=3) and P (n=1)
Jin et al. (2010)	Case report (1)	+		T
Bovenschen (2009)	Case report (1)	+		T
Erkek et al. (2007)	Case report (1)	+		T + P
Connolly et al. (2004)	Case report (1)	+		T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Cheilitis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 12

- 2 excluded at title/abstract filtering stage:
 - 1 non-target disorder
 - 1 no TCI exposure

Selected full citations:

- Yamaguchi Y et al. Plasma Cell Cheilitis Successfully Treated with Topical Calcineurin Inhibitors. *Eur J Dermatol* 2016;26(6):609-610.
- Apalla Z et al. Psoriatic cheilitis: A Report of 2 Cases Treated Successfully with Topical Tacrolimus and a Review of the Literature. *Actas Dermosifiliogr* 2015;106(8):687-689.
- da Cunha Filho RR et al. "Angular" Plasma Cell Cheilitis. *Dermatol Online J* 2014;20(3)
- Yoshimura K et al. Successful Treatment with 308-nm Monochromatic Excimer Light and Subsequent Tacrolimus 0.03% Ointment in Refractory Plasma Cell Cheilitis. *J Dermatol* 2013;40(6):471-4
- Hanami Y et al. Successful Treatment of Plasma Cell Cheilitis with Topical Tacrolimus: Report of Two Cases. *Dermatol Online J* 2011;17(2):6
- Choi JW et al. Successful Treatment of Plasma Cell Cheilitis with Topical Calcineurin Inhibitors. *J Dermatol* 2009;36(12):669-71
- Jin SP et al. Plasma Cell Cheilitis, Successfully Treated with Topical 0.03% Tacrolimus Ointment. *J Dermatolog Treat* 2010;21(3):130-2.
- Bovenschen HJ. Novel Treatment for Cheilitis Glandularis. *Acta Derm Venereol* 2009;89(1):99-100.
- Erkek E et al. A Case of Cheilitis Glandularis Superimposed on Oral Lichen Planus: Successful Palliative Treatment with Topical Tacrolimus and Pimecrolimus. *J Eur Acad Dermatol* 2007;21(7):999-1000.
- Connolly M, Kennedy C. Exfoliative Cheilitis Successfully Treated with Topical Tacrolimus. *Br J Dermatol* 2004;151(1):241-2

Confluent and reticulated papillomatosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Tirado-Sanchez (2013)	Case report ()	+	1	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Confluent papillomatosis OR Reticulated papillomatosis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 2

- 1 excluded at title/abstract filtering stage: (non-exposure to TCIs)

Selected full citations:

1. Tirado-Sanchez A, Ponce-Olivera RM. Tacrolimus in confluent and reticular papillomatosis of Gougerot Carteaud. Int J Dermatol 2013;52(4):513-514.

Cutaneous mastocytosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Correia et al. (2010) Avshalumov et al (2008) Lee et al. (2005)	Case series (2) Case report (1) Case report (1)	+	4	P T P
Evidence of harm				

Lack of effect				
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P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Cutaneous mastocytosis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 3

Selected full citations:

- Correia O et al. Cutaneous Mastocytosis: Two Pediatric Cases Treated with Topical Pimecrolimus. *Dermatol Online J* 2010;16(5):8
- Avshalumov K et al. Bullous Mastocytosis: Report of a Patient and a Brief Review of the Literature. *Am J Dermatopathol* 2008;30(5):455-457
- Lee HW et al. Two Cases of Telangiectasia Macularis Eruptiva Perstans Demonstrated by Immunohistochemistry for c-kit (CD 117). *J Dermatol* 2005;32(10):817-820

Darier disease

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				

Level 3 evidence: Lu et al (2011) Rubegni et al (2006)	Case report (1) Case report (1)	+	2	P T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Darier disease)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 5

- 3 excluded at title/abstract filtering stage:
 - 3 due to non-target disorder

Selected full citations:

1. Lu Y et al. A Case of Facial Keratosis Follicularis Squamosa Resembling Atrophic Acne Scarring, Successfully Treated with Topical Pimecrolimus. Indian J Dermatol Venereol Leprol 2011;77(1):69-70
2. Rubegni P et al. A Case of Darier's Disease Successfully Treated with Topical Tacrolimus. J Eur Acad Dermatol Venereol 2006;20(1):84-87.

Eosinophilic pustular folliculitis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Zitelli et al (2015) Patel et al (2012) Rho & Kim (2007) Hara et al (2004) Kabashima et al (2004) Dale & Shaw (2000)	Case report (1) Case series (2) Case report (1) Case report (1) Case report (1) Case report (1) Case report (1)	++ + + + + + +	7	T T P T T T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Eosinophilic pustular folliculitis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 6

Selected full citations:

- Zitelli K et al. Eosinophilic Folliculitis Occurring after Stem Cell Transplant for Acute Lymphoblastic Leukemia: a Case Report and Review. *Int J Dermatol* 2015;54(7):785-789.
- Patel NP et al. Treatment of Eosinophilic Pustulosis of Infancy with Topical Tacrolimus. *Br J Dermatol* 2012;167(5):1189-91.
- Rho NK, Kim BJ. Eosinophilic Pustular Folliculitis: Successful Treatment with Topical Pimecrolimus. *Clin Exp Dermatol* 2007;32(1):108-109.
- Hara D et al. Treatment of Eosinophilic Pustular Folliculitis with Tacrolimus Ointment. *J Am Acad Dermatol* 2004;51(5 Suppl):S143-5.
- Kabashima K et al. Treatment of Eosinophilic Pustular Folliculitis (Ofuji's Disease) with Tacrolimus Ointment. *Br J Dermatol* 2004;151(4):949-50.
- Dale S, Shaw J. Clinical Picture. Eosinophilic Pustular Folliculitis. *Lancet* 2000;356(9237):1235.

Erosive pustular dermatosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Zahdi et al (2013) Vano-Galvan et al (2012) Tardio & Daly (2011) Dall'Olio et al (2011) Seckin et al (2009) Tavares-Bello (2009) Marzano et al (2009) Cenkowski & Silver (2007) Patton et al (2007) Séez et al (2005) Brouard et al (2002)	Case report (1) Case report (1) Case report (1) Case series (2) Case series (2) Case report (1) Case report (1) Case report (1) Case report (1) Case series (11) Case report (1) Case series (3)	+	25	T T T T P T T T T T T T
Evidence of harm				

Lack of effect				
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P, pimecrolimus; T, tacrolimus; TCS, topical corticosteroids

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Erosive pustular dermatosis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 12

- 1 excluded at title/abstract filtering stage:
 - 1 no access to full article

Selected full citations:

1. Zahdi MR et al. Erosive pustular dermatosis of the scalp successfully treated with oral prednisone and topical tacrolimus. *An Bras Dermatol* 2013;88(5):796-798.
2. Vano-Galvan S et al. Erosive pustular dermatosis of the scalp. *J Pak Med Assoc* 2012;62(5):501-502.
3. Tardio NB, Daly TJ. Erosive pustular dermatosis and associated alopecia successfully treated with topical tacrolimus. *J Am Acad Dermatol* 2011;65(3):93-94.
4. Dall'Olio E et al. Erosive pustular dermatosis of the leg: Long-term control with topical tacrolimus. *Australas J Dermatol* 2011;52(1):15-17.
5. Seckin D et al. Erosive pustular dermatosis of the leg: An overlooked entity? *J Cutan Med Surg* 2009;13(3):160-163.
6. Tavares-Bello R. Erosive Pustular Dermatosis of the Scalp. A chronic recalcitrant dermatosis developed upon C02 laser treatment. *Dermatology* 2009;219(1):71-72.

7. Marzano AV et al. Localized erosive pustular dermatosis of the scalp at the site of a cochlear implant: Successful treatment with topical tacrolimus. *Clin Exp Dermatol* 2009;34(5):157-159.
8. Cenkowski MJ, Silver S. Topical tacrolimus in the treatment of erosive pustular dermatosis of the scalp. *J Cutan Med Surg* 2007;11(6):222-225.
9. Patton D et al. Chronic atrophic erosive dermatosis of the scalp and extremities: A recharacterization of erosive pustular dermatosis. *J Am Acad Dermatol* 2007;57(3):421-427.
10. Séez M et al. Successful treatment of erosive pustular dermatosis of the scalp with topical tacrolimus. *Clin Exp Dermatol* 2005;30(5):599-600.
11. Brouard MC et al. Erosive pustular dermatosis of the leg: Report of three cases. *Br J Dermatol* 2002;147(4):765-769.

Erythema annulare centrifugum

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Rao & Paliser 2003	Case series (2)	+	2	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Erythema annulare centrifugum)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 4

- 3 excluded at title/abstract filtering stage:
 - 3 due to non-target disorder

Selected full citations:

1. Rao NG, Pariser RJ. Annular erythema responding to tacrolimus ointment. J Drugs Dermatol 2004;2(4):421-4.

Follicular mucinosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Kluk et al (2014) Gorpelioglu et al (2009)	Case report (1) Case report (1)	+ +	2	T P
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Follicular mucinosis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 3

- 1 excluded at title/abstract filtering stage:
 - 1 due to no exposure due to TCI

Selected full citations:

1. Kluk J et al. Follicular mucinosis treated with topical 0.1% tacrolimus ointment. Clin Exp Dermatol 2014;39(2):227-228.
2. Gorpelioglu C et al. A case of follicular mucinosis treated successfully with pimecrolimus. Clin Exp Dermatol 2009;34(1):86-87.

Folliculitis, eosinophilic pustular

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Zitelli et al (2015) Rho & Kim (2007) Gesierich et al (2006) Toutous-Trellu (2005) Hara et al (2004)	Case report (1) Case report (1) Case report (1) Case series (2) Case report (1)	+	8	T P T T T

Kabashima et al (2004) Dale et al (2000)	Case report (1) Case report (1)	+		T T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Folliculitis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 16

- 9 excluded at title/abstract filtering stage:
 - 3 due to animal study
 - 5 due to non-target disorder
 - 1 non-systematic review

Selected full citations:

1. Zitelli J et al. Eosinophilic folliculitis occurring after stem cell transplant for acute lymphoblastic leukemia: a case report and review. *Int J Dermatol* 2015;54(7):785-9.
2. Rho NK, Kim BJ. Eosinophilic pustular folliculitis: successful treatment with topical pimecrolimus. *Clin Exp Dermatol* 2007;32(1):108-9.
3. Gesierich A et al. Eosinophilic folliculitis in a Caucasian patient: association with toxocariasis? *J Eur Acad Dermatol Venereol* 2006;20(10):1317-21.

4. Toutous-Trellu L et al. Topical tacrolimus for effective treatment of eosinophilic folliculitis associated with human immunodeficiency virus infection. *Arch Dermatol* 2005;141(10):1203-8.
5. Hara D et al. Treatment of eosinophilic pustular folliculitis with tacrolimus ointment. *J Am Acad Dermatol* 2004;51(5 Suppl):S143-5.
6. Kabashima K et al. Treatment of eosinophilic pustular folliculitis (Ofuji's disease) with tacrolimus ointment. *Br J Dermatol* 2004;151(4):949-50.
7. Dale S, Shaw J. Clinical picture. Eosinophilic pustular folliculitis. *Lancet* 2000;356(9237):1235.

Folliculitis decalvans

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Bastida et al (2012)	Case series (4)	+	4	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Folliculitis decalvans)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French

3) Species: Humans

Total articles retrieved: 1

Selected full citations:

1. Bastida J et al. Treatment of folliculitis decalvans with tacrolimus ointment. Int J Dermatol 2012;51(2):216-220.

Fox-Fordyce disease

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Milcic & Nikolic (2012) Pock et al 2006 Kaya Erdogan et al (2015)	Case report (1) Case report (3) Case series (1)	++ + +	5	P P T
Evidence of harm				
Lack of effect Kaya Erdogan et al (2015)	Case report (1)	0	1	T

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Fox-Fordyce disease)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 4

- 1 excluded at title/abstract filtering stage: non-systematic review

Selected full citations:

1. Milcic D, Nikolic M. Clinical effects of topical pimecrolimus in a patient with Fox- Fordyce disease. Austraslas J Dermatol 2012; 53(2):e34-5.
2. Pock L et al. Pimecrolimus is effective in Fox-Fordyce disease. Int J Dermatol 2006; 45(9):1134-1135.
3. Kaya Erdogan H et al. Clinical effects of topical tacrolimus on Fox-Fordyce disease. Case Rep Dermatol Med 2015;2015:205418.

Geographic Tongue

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Purani & Purani (2014) Ishibashi et al. (2010)	Case report (1) Case series (2)	+ +	3	T T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Geographic tongue)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 3

- 2 excluded at title/abstract filtering stage:
 - 1 due to wrong disease
 - 1 due to wrong medication

Selected full citations:

1. Purani JM, Purani HJ. Treatment of geographic tongue with topical tacrolimus. BMJ Case rep 2014; bcr-2013-201268.

Articles identified through manual search:

2. Ishibashi M et al. Geographic tongue treated with topical tacrolimus. J Dermatol Case Rep 2010;4(4):57-9.

Granuloma annulare

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Gomez-Moyano et al (2014) Lopez-Navarro et al (2008)	Case report: TAC (1) Case report: TAC (1)	+ +	13	T T

Baskan et al (2007) Lee et al (2005) Rigopoulos et al (2005) Jain & Stephens (2004) Harth & Linse (2004)	Case report: PIM (1) Case report: PIM (1) Case report: PIM (1) Case series: TAC (4) Case series: TAC (4)	+		P P P T T
Evidence of harm				
Lack of effect Rallis et al (2009) Harth & Linse (2004)	Case series: TAC (3) Case series: TAC (2)	0 0	5	T T

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Granuloma annulare)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 10

- 2 excluded at title/abstract filtering stage:
 - 2 due to no exposure to TCI

Selected full citations:

1. Gomez-Moyano E et al. Periorbital granuloma annulare successfully treated with tacrolimus 0.1% ointment. Int J Dermatol 2014;53(2):156-157.

2. Rallis E et al. Granuloma annulare of childhood successfully treated with potent topical corticosteroids previously unresponsive to tacrolimus ointment 0.1%: Report of three cases. *Clin Exp Dermatol* 2009;34(7):475-476.
3. Lopez- Navarro N et al. Successful treatment of perforating granuloma annulare with 0.1% tacrolimus ointment. *J Dermatolog Treat* 2008;19(6):376-377.
4. Baskan EB et al. A case of generalized granuloma annulare with myelodysplastic syndrome: successfully treatment with systemic isotretinoin and topical pimecrolimus 1% cream combination. *J Eur Acad Dermatol Venereol* 2007;21(5):693-695.
5. Lee HW et al. Annular elastolytic giant cell granuloma in an infant: improvement after treatment with oral tranilast and topical pimecrolimus. *J Am Acad Dermatol* 2005;53(5 Suppl 1):244-246.
6. Rigopoulos D et al. Pimecrolimus 1% cream in the treatment of disseminated granuloma annulare. *Br J Dermatol* 2005;152(6):1364-1365.
7. Jain S, Stephens CJ. Successful treatment of disseminated granuloma annulare with topical tacrolimus. *Br J Dermatol* 2004;150(5):1042-1043.
8. Harth W, Linse R. Topical tacrolimus in granuloma annulare and necrobiosis lipoidica. *Br J Dermatol* 2004;150(4):792-794.

Granuloma faciale

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				

Level 3 evidence:			13	
Mitchell (2004)	Case report (1)	+		T
Gupta et al (2012)	Case report (1)	+		T
Santos-Alarcon et al (2016)	Case report (1)	+		T
Lima et al (2015)	Case report (1)	+		T
Dourmishev et al (2014)	Case report (1)	+		P
Cecchi et al (2010)	Case report (1)	+		T
Pérez-Robanya et al (2009)	Case report (1)	+		T
Patterson & Coutts (2009)	Case report (1)	+		T
Tomson et al (2009)	Case report (1)	+		T
Jedlicková et al (2008)	Case report (1)	+		T
Marcoval et al (2006)	Case report (1)	+		T
Eetam et al (2006)	Case report (1)	+		P
Ludwig et al (2003)	Case report (1)	+		T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Granuloma faciale)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 14

- 3 excluded at title/abstract filtering stage:

- 1 non-target disorder
- 1 no access to full text
- 1 systemic review on granuloma faciale in general, not on TCIs

Selected full citations:

1. Santos-Alacron S et al. Granuloma faciale treatment with tacrolimus. Dermatol Online J 2016;22(7): pii: 13030/qt92n4f40x.
2. Lima RS et al. Granuloma faciale: a good therapeutic response with the use of topical tacrolimus. An Bras Dermatol 2015; 90(5):735-737.
3. Dourmishev L et al. Granuloma faciale effectively treated with topical pimecrolimus. Acta Dermatovenerol Croat 2014; 22(4):305-307.
4. Cecchi R et al. Topical tacrolimus in the treatment of granuloma faciale. Int J Dermatol 2010;49(12):1463-1465.
5. Pérez-Robanya N et al. Successful response to topical tacrolimus for a granuloma faciale in an elderly patient. Dermatol 2009;219:359-360.
6. Patterson C, Coutts. Granuloma faciale successfully treated with topical tacrolimus. Australas J Dermatol 2009;50(3):217-219.
7. Tomson N et al. Granuloma faciale treated successfully with topical tacrolimus. Clin Exp Dermatol 2009;34(3):424-425.
8. Jedlicková H et al. Granuloma faciale successfully treated with topical tacrolimus: A case report. Acta Dermatovenerol Alp Pannonica Adriat 2008; 17(10):34-36.
9. Maroval J et al. Granuloma faciale: treatment with topical tacrolimus. J Am Acad Dermatol 2006; 55(Suppl 5):S110-111.
10. Eetam I et al. Granuloma faciale: is it a new indication for pimecrolimus? A case report. J Dermatolog Treat 2006;17(4):238-240.
11. Ludwig E et al. New treatment modalities for granuloma faciale. Br J Dermatol 2003;149(3):634-637.

Articles sourced through manual searches:

12. Mitchell D. Successful treatment of granuloma faciale with tacrolimus. Dermatol Online J 2004;10:23.
13. Gupta L et al. Granuloma faciale with extrafacial involvement and response to tacrolimus. J Cutan Aesthet Surg 2012;5(2):150-152.

Hailey-Hailey disease

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				

Level 2 evidence:				
Level 3 evidence:				
Tchernev & Cardoso (2011)	Case report (1)	+	6	P
Persić-Vojinović et al (2006)	Case report (1)	+		T
Rocha Paris et al (2005)	Case report (1)	+		T
Reuter et al (2005)	Case report (1)	+		T
Sand & Thomsen (2003)	Case report (1)	+		T
Rabeni & Cunningham (2002)	Case report (1)	+		T
Evidence of harm				
Lack of effect				
Pagliarello et al (2012)	Case report (1)	0	2	T
Laffitte & Panizzon (2004)	Case report (1)	0		T

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Hailey-Hailey disease)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 15

- 6 excluded at title/abstract filtering stage:
 - 2 excluded due to non-target disorder
 - 2 excluded due to no access to full text

- 2 excluded due to other medication

Selected full citations:

1. Pagliarello C et al. Topical tacrolimus and 50% zinc oxide paste for Hailey-Hailey disease: less is more. *Acta Derm Venereol* 2012;92(4):437-438.
2. Tchernev G, Cardoso JC. Familial benign chronic pemphigus (Hailey-Hailey disease): use of topical immunomodulators as a modern treatment option. *Rev Med Chil* 2011;139(5):633-6377.
3. Hurd DS et al. A case report of Hailey-Hailey disease treated with alefacept (Amevive). *Br J Dermatol* 2008;158(2):399-401.
4. Persić-Vojinović S et al. Disseminated Hailey-Hailey disease treated with topical tacrolimus and oral erythromycin: Case report and review of the literature. *Acta Dermatovenerol Croat* 2006;14(4):253-257.
5. Rocha Paris F et al. Topical tacrolimus in Hailey-Hailey disease. *Int J Tissue React* 2005;27(4):151-4.
6. Reuter J et al. Tacrolimus—a new therapeutic option for Hailey-Hailey -disease? *J Dtsch Dermatol Ges* 2005;3(4):278-279.
7. Laffitte E, Panizzon RG. Is topical tacrolimus really and effective therapy for Hailey-Hailey disease? *Arch Dermatol* 2004;140(10):1282
8. Sand C, Thomsen HK. Topical tacrolimus ointment is an effective therapy for Hailey-Hailey disease. *Arch Dermatol* 2003;139(11):1401-1402.
9. Rabeni EJ, Cunningham NM. Effective treatment of Hailey-Hailey disease with topical tacrolimus. *J Am Acad Dermatol* 2002;47(5):797-798.

Inflammatory linear verrucous epidermal nevus

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Akelma et al (2013) Mutasim (2006)	Case report (1) Case report (1)	+	2	P T
Evidence of harm				

Lack of effect				
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P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Inflammatory linear verrucous epidermal nevus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 2

Selected full citations:

1. Akelma AZ et al. A diagnostic dilemma: inflammatory linear verrucous epidermal nevus versus linear psoriasis. *J Pediatr* 2013;162(4):879.
2. Mutasim DF. Successful treatment of inflammatory linear verrucous epidermal nevus with tacrolimus and fluocinonide. *J Cutan Med Surg* 2006;10(1):45-47.

Jellyfish stings

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Loredana Asztalos et al (2014)	Case report (1)	+	4	T

Di Costanzo et al (2009) Rallis & Limas (2007) Ulrich et al (2007)	Case report (1) Case report (1) Case report (1)	+		P T T
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Jellyfish stings)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 4

Selected full citations:

1. Loredana Asztalos M et al. Recurrent dermatitis and dermal hypersensitivity following jellyfish sting: a case report and review of literature. *Pediatr Dermatol* 2014;31(2):217-9.
2. Di Costanzo L et al. Successful management of a delayed and persistent cutaneous reaction to jellyfish with pimecrolimus. *J Dermatolog Treat* 2009;20(3):179-180.
3. Rallis E, Limas C. Recurrent dermatitis after solitary envenomation by jellyfish partially responded to tacrolimus ointment 0.1%. *J Eur Acad Dermatol Venereol* 2007;21(9):1287-8.
4. Ulrich H et al. Granulomatous jellyfish dermatitis. *J Dtsch Dermatol Ges* 2007;5(6):493-495.

Jessner lymphocytic infiltrate

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Tzung & Wu (2005)	Case report (1)	+	1	P (good response following failure of T)
Evidence of harm				
Lack of effect Tzung & Wu (2005)	Case report (1)			T (initial response for 2 wks then worsening)

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Jessner lymphocytic infiltrate)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

2) Language: English, French

3) Species: Humans

Total articles retrieved: 1

Selected full text articles:

1. Tzung TY, Wu JC. Topical calcineurin inhibitors in treating Jessner's lymphocytic infiltration of the skin: report of a case. Br J Dermatol 2005;152(2):383-4.

Juvenile plantar dermatosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Shipley & Kennedy (2006)	Case report (1)	+	1	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Juvenile plantar dermatosis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 1

Selected full citations:

1. Shipley DR, Kennedy CT. Juvenile plantar dermatosis responding to topical tacrolimus ointment. Clin Exp Dermatol 2006;31(3):453-454.

Lichen myxedematosus

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Rongioletti et al (2008) Sulit et al (2005)	Case series (2) Case report (1)	+ +	3	T P
Evidence of harm				
Lack of effect				

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (lichen myxedematosus)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 2

Selected full citations:

1. Rongioletti F et al. Treatment of localized lichen myxedematosus of discrete type with tacrolimus ointment. *J Am Acad Dermatol* 2008;58(3):530-532.
2. Sulit DJ et al. Discrete papular form of lichen myxedematosus: a case report and review of the literature. *Cutis* 2005;75(2):105-112.

Lichen nitidus

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Lee et al (2013) Farshi & Mansouri (2011) Dobbs & Murphy (2004) Cho et al (2014)	Case report: PIM (1) Case report: PIM (1) Case report: TAC (1) Case series: TAC (1)	++ + + +	4	P P T T
Evidence of harm				
Lack of effect Cho et al (2014)	Case report (1)	0	1	T

P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Lichen nitidus)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 5

- 1 excluded at title/abstract filtering stage:
 - No access to full article

Selected full citations:

1. Lee WJ et al. Penile lichen nitidus successfully treated with topical pimecrolimus 1% cream. *J Dermatol* 2013;40(6):499-500.
2. Farshi S, Mansouri P. Letter: Generalized lichen nitidus successfully treated with pimecrolimus 1 percent cream. *Dermatol Online J* 2011;17(7):11.
3. Dobbs CR, Murphy SJ. Lichen nitidus treated with topical tacrolimus. *J Drugs Dermatol* 2004;3(6):683-684.
4. Cho EB et al. Three cases of lichen nitidus associated with various cutaneous diseases. *Ann Dermatol* 2014;26(4):505-9.

Lymphocytoma cutis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: El-Dars et al (2005)	Case series (2)	+	2	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Lymphocytoma cutis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 2

- 1 excluded at title/abstract filtering stage (non-target disorder)

Selected full citations:

1. El-Dars LD et al. Lymphocytoma cutis treated with topical tacrolimus. Clin Exp Dermatol 2005;30(3):305-7.

Necrobiosis lipoidica

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Ginocchio et al (2017) Koura-Nishiura et al (2016) Binamer et al (2012) Harth & Linse (2004) Clayton (2005)	Case report (1) Case report (1) Case series (2) Case series (2) Case report (1)	+	7	T T T T T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Necrobiosis lipoidica)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 8

- 3 excluded at title/abstract filtering stage:
 - 1 no exposure to TCIs
 - 1 unable to access full text
 - 1 article in German

Selected full citations:

1. Ginocchio L et al. Refractory ulcerated necrobiosis lipoidica: Closure of a difficult wound with topical tacrolimus. *Adv Skin Wound Care* 2017;30(10):469-472.
2. Koura-Nishiura A et al. Clearance of atypical facial necrobiosis lipoidica with tacrolimus ointment. *J Eur Acad Dermatol Venereol* 2016;30(2):383-385.
3. Binamer Y et al. Treatment of ulcerative necrobiosis lipoidica with topical calcineurin inhibitor: case report and literature review. *J Cutan Med Surg* 2012;16(6):458-61.
4. Harth W, Linse R. Topical tacrolimus in granuloma annulare and necrobiosis lipoidica. *Br J Dermatol* 2004;150(4):792-4.
5. Clayton TH, Harrison PV. Successful treatment of chronic ulcerated necrosis lipoidica with 0.1% topical tacrolimus ointment. *Br J Dermatol.* 2005 Mar;152(3):581-2.

Necrolytic acral erythema

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Manzur & Siddiqui (2008)	Case report (1)	+	1	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Necrolytic acral erythema)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 1

Selected full citations:

1. Manzur A, Siddiqui AH. Necrolytic acral erythema: successful treatment with topical tacrolimus ointment. Int J Dermatol 2008;47(8):1073-1075.

Peristomal skin disease

Citations	Type of evidence (n-value for each)	Result	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Wells et al (2006)	Case series (3)	+	3	T
Lack of effect:				
Evidence of harm:				

T: tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus) and (periostomal skin care)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 1

Selected full citations:

1. Wells GL et al. Tacrolimus ointment 0.1% for the treatment of peristomal skin disease: 3 case reports. Cutis 2006;78(4):258-60.

Pityriasis lichenoides chronica, varioliformis acuta

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Mallipeddi & Evans (2003) Di Costanza (2009) Simon et al. (2004)	Case report (1) Case report (1) Case report (2)	++ + +	4	T T T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Pityriasis lichenoides chronica)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews

- 2) Language: English, French
- 3) Species: Humans

Total articles retrieved: 3

Selected full citations:

1. Mallipeddi R, Evans AV. Refractory pityriasis lichenoides chronica successfully treated with topical tacrolimus. Clin Exp Dermatol 2003;28(4):456-458.
2. Di Costanzo L et al. Successful association in the treatment of pityriasis lichenoides et varioliformis acuta. JEADV 2009;23:971-2.

3. Simon D et al. Successful treatment of pityriasis lichenoides with topical tacrolimus. Br J Dermatol 2004;150:1033-5.

Pustular psoriasis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Laino & Dicarlo (2011) Brill et al (2005) Rodríguez García et al (2005) Wilsmann- Theis et al (2004) Ishiko et al. (2003)	Case series (2) Case report (1) Case report (1) Case series (2) Case report (1)	++ + + + +	7	T T T T T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (pustular psoriasis)

Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 11

- 6 excluded at title/abstract filtering stage:

- 6 no exposure to TCIs

Selected full citations:

1. Laino L, DiCarlo A. Palmoplantar pustular psoriasis: Clinical and video thermographic evaluation before and after topical tacrolimus treatment. *Arch Dermatol* 2011;147(6):760.
2. Brill TJ et al. Successful treatment of acrodermatitis continua of Hallopeau with sequential combination of calcipotriol and tacrolimus ointments. *Dermatology* 2005;211(4):351-355.
3. Rodríguez García F et al. Generalized pustular psoriasis successful treated with topical tacrolimus. *Br J Dermatol* 2005;152(3):587-588.
4. Wilsmann-Theis D et al. Successful treatment of acrodermatitis continua suppurativa with topical tacrolimus 0.1% ointment. *Br J Dermatol* 2004;150(6):1194-1197.
5. Ishiko A et al. A case of generalized pustular psoriasis treated with topical tacrolimus. *Arch Dermatol* 2003;139:1219.

Reactive arthritis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Bakkour et al (2014) Herrera-Esparza et al (2009)	Case report (1) Case series (4)	+ +	5	T T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Reactive arthritis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 3

- 1 excluded at title/abstract filtering stage (due to non-target disorder)

Selected full citations:

1. Bakkour W et al. Successful use of dapson for the management of circinate balanitis. Clin Exp Dermatol 2014;39(3):333-335.
2. Herrera-Esparza R et al. Tacrolimus therapy for circinate balanitis associated with reactive arthritis. J Clin Rheumatol 2009;15(8):377-379.

Red baby

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: Leonardi et al (2006)	Case report (1)	+	1	T
Evidence of harm				
Lack of effect				

T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (red baby)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
2) Language: English, French
3) Species: Humans

Total articles retrieved: 1

- 0 excluded at title/abstract filtering stage

Selected full citations:

1. Leonardi S et al. Efficacy and safety of tacrolimus ointment 0.03% treatment in a 1-month old “red baby”: a case report. Allergy Asthma Proc 2006;27(6):523-6.

Sarcoidosis

Citations	Type of evidence (n-value for each)	Results	Total population studied*	Notes
Level 1 evidence:				
Level 2 evidence:				
Level 3 evidence: La Placa et al (2015) Landers et al (2005) Gutzmer et al (2003) Katoh et al (2002) Tammaro et al. (2014) Green et al. (2007)	Case report (1) Case report (1) Case report (1) Case report (1) Case report (1) Case report (1) Case report (1)	+	6	P T T T P T
Evidence of harm				

Lack of effect Mahnke et al (2003)	Case report (1)	0	1	
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P, pimecrolimus; T, tacrolimus

+: positive evidence for efficacy; +/-: partial efficacy (e.g. one body location only); 0: lack of effect; -: evidence of harm

*Total population studied includes only subjects exposed to TCI.

PubMed literature search terms: (topical calcineurin inhibitor OR tacrolimus ointment OR tacrolimus cream OR pimecrolimus OR TCI) and (Sarcoidosis)

- Filters: 1) Article type: clinical trials, case reports, guidelines, meta-analyses, systematic reviews
 2) Language: English, French
 3) Species: Humans

Total articles retrieved: 16

- 10 excluded at title/abstract filtering stage:
 - 5 non-target disorder
 - 3 no TCI exposure
 - 2 no access to full text

Selected full citations:

1. La Placa M et al. Disfiguring popular sarcoidosis of the face: dramatic improvement with pimecrolimus. *J Eur Acad Dermatol Venereol* 2015;29(12):2497-2499.
2. Landers MC et al. Cutaneous and pulmonary sarcoidosis in association with tattoos. *Cutis* 2005;75(1):44-48.
3. Gutzmer R et al. Successful topical treatment of cutaneous sarcoidosis with tacrolimus. *Hautarzt* 2003; 54(12):1193-1197.
4. Mahnke N et al. Medium Dose UV-A1 phototherapy. Successful treatment of cutaneous sarcoidosis. *Hautarzt* 2003;54(4):364-366.
5. Katoh N et al. Cutaneous sarcoidosis successfully treated with topical tacrolimus. *Br J Dermatol* 2002;147(1):154-156.
6. Green et al. Topical tacrolimus for the treatment of cutaneous sarcoidosis. *Clin Exp Dermatol* 2007;32:457-8.

Articles identified through manual searches:

1. Tammaro A et al. Topical Pimecrolimus as a New Optional Treatment in Cutaneous Sarcoidosis of Lichenoid Type. Case Rep Dermatol Med 2014:976851.