

Appendix

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Appendix A. Search Strategy

Search 1: MEDLINE® and Cochrane Central Register of Controlled Trials (OVID)

1. psoriasis.mp. or Psoriasis/
2. Psoriasis/ or plaque psoriasis.mp.
3. 1 or 2
4. methotrexate.mp. or Methotrexate/
5. cyclosporin.mp. or Cyclosporine/
6. cyclosporine.mp. or Cyclosporine/
7. ciclosporin.mp. or Cyclosporine/
8. calcineurin inhibitor.mp.
9. acitretin.mp. or Acitretin/
10. retinoids.mp. or Retinoids/
11. antimalarials.mp. or Antimalarials/
12. hydroxyurea.mp. or Hydroxyurea/
13. isotretinoin.mp. or Isotretinoin/
14. sulfasalazine.mp. or Sulfasalazine/
15. 6-thioguanine.mp. or Thioguanine/
16. azathioprine.mp. or Azathioprine/
17. cyclophosphamide.mp. or Cyclophosphamide/
18. mycophenolate mofetil.mp.
19. nsaid.mp. or Anti-Inflammatory Agents, Non-Steroidal/
20. antihistamine.mp. or Histamine Antagonists/
21. leflunomide.mp.
22. tacrolimus.mp. or Tacrolimus/
23. fish oil.mp. or Fish Oils/
24. ergocalciferols.mp. or Ergocalciferols/
25. bicillin l-a.mp. or Penicillin G Benzathine/
26. prednisone.mp. or Prednisone/
27. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28. etanercept.mp.
29. infliximab.mp.
30. adalimumab.mp.
31. alefacept.mp.
32. ustekinumab.mp.
33. cnto 1275.mp.
34. biologics.mp.
35. biologic agents.mp.
36. monoclonal antibody.mp. or Antibodies, Monoclonal/
37. t-cell modulator.mp.
38. tumor necrosis factor inhibitor.mp.
39. briakinumab.mp.
40. ABT 874.mp.
41. voclosporin.mp.
42. ISA-247.mp.

43. CP 690,550.mp.
44. certolizumab.mp.
45. cdp870.mp.
46. daclizumab.mp.
47. erlotinib.mp.
48. abatacept.mp.
49. rituximab.mp.
50. golimumab.mp.
51. 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
52. psoralen.mp. or Ficusin/
53. PUVA Therapy/ or puva.mp.
54. phototherapy.mp. or Phototherapy/
55. uvb.mp.
56. uva.mp.
57. laser therapy.mp. or Laser Therapy/
58. Lasers, Excimer/ or excimer.mp.
59. goeckerman.mp.
60. ingram.mp.
61. 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60
62. 51 and 61
63. 3 and 62
64. 27 and 51
65. 3 and 64
66. 63 or 65

Search 2: MEDLINE®, The Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, and Health Technology Assessment database

1. randomized controlled trials/
2. controlled clinical trial.sh.
3. clinical trial/
4. randomi\$ control\$ trial\$.tw.
5. clinical trial\$.tw.
6. trial\$.tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. review literature/
9. meta-analysis.sh.
10. meta-analy\$.tw.
11. metaanaly\$.tw.
12. (meta adj analy\$).tw.
13. 8 or 9 or 10 or 11 or 12
14. (indirect adj2 comparison\$).tw.
15. (indirect adj2 evaluat\$).tw.
16. (indirectly adj2 compar\$).tw.
17. bayesian.tw.
18. (mixed treatment adj compar\$).tw.

19. (mixed treatment adj evaluat\$).tw.
20. MTC.tw.
21. 14 or 15 or 16 or 17 or 18 or 19 or 20
22. 7 and 13
23. 21 and 22
24. psoriasis.mp. [mp=ps, rs, ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct]
25. psoriasis/
26. chronic psoriasis.mp. [mp=ps, rs, ti, ot, ab, nm, hw, ui, an, tx, kw, sh, ct]
27. 24 or 25 or 26
28. 23 and 27
29. remove duplicates from 28

Appendix B. Data Extraction Form

Study Identification

Unique ID:	First author's name, publication year:	Study acronym (if applicable):	Publication format: <input type="checkbox"/> Full text manuscript <input type="checkbox"/> Abstract <input type="checkbox"/> Other (specify):	
Funding Source (specify): <input type="checkbox"/> Industry <input type="checkbox"/> Government/Foundation <input type="checkbox"/> Academia <input type="checkbox"/> Other/NR	Conflicts of interest reported? Y <input type="checkbox"/> Not reported <input type="checkbox"/>	Geographic location and setting:	Number of Centers:	Total N randomized (N randomized in arms we use):

Study Design and Quality Characteristics

(Select either RCT or observational and complete corresponding section, if you answer N report why)

<input type="checkbox"/> Randomized controlled trial <input type="checkbox"/> Before and after study	
Were the groups similar baseline in terms of baseline characteristics? Y <input type="checkbox"/> N <input type="checkbox"/> Not reported <input type="checkbox"/>	Were outcomes assessed using a valid methodology and criteria? Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> Not reported <input type="checkbox"/>
Were subjects and providers blind to intervention status of participants? Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> Not reported <input type="checkbox"/>	Were outcome assessors blind to intervention status? Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> Not reported <input type="checkbox"/>
Randomization technique described: 	Outcome assessment described (Who and How):
Was intention to treat analysis used? Y <input type="checkbox"/> N <input type="checkbox"/>	
Were methods used for randomization adequate? Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> Not reported <input type="checkbox"/>	Was incomplete data adequately addressed? Y <input type="checkbox"/> N <input type="checkbox"/> Not reported <input type="checkbox"/>

Was allocation concealment adequate? Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> Not reported <input type="checkbox"/>			
Was the differential loss to followup between groups <10%? Y <input type="checkbox"/> N <input type="checkbox"/>		Was the overall loss to followup <20%? Y <input type="checkbox"/> N <input type="checkbox"/>	
Duration of followup (longest):		Follow-up % for the primary outcome: Intervention Comparator	
Overall quality score (use protocol for criteria): good <input type="checkbox"/> fair <input type="checkbox"/> poor <input type="checkbox"/>			
<input type="checkbox"/> Controlled observational study (specify design in detail): <input type="checkbox"/> Case-control <input type="checkbox"/> Cohort <input type="checkbox"/> Other (specify)			
Unbiased selection of cohort: Y <input type="checkbox"/> N <input type="checkbox"/> NR <input type="checkbox"/>	Selection minimizes baseline differences: Y <input type="checkbox"/> N <input type="checkbox"/> NR <input type="checkbox"/>	Blinded outcome assessment: Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>	Outcome assessment described:
Sample size calculated: Y <input type="checkbox"/> N <input type="checkbox"/> NR <input type="checkbox"/>	Adequate description of cohort: Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>	Validated method to ascertain exposure (CC): Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>	Validated method to ascertain outcomes: Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>
Adequate follow-up period: Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>	ITT for cohort: Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>	Adequate analysis to control for confounding: Y <input type="checkbox"/> N <input type="checkbox"/> Partially <input type="checkbox"/> NR <input type="checkbox"/>	Covariates/potential confounders adjusted for:
Selection of comparison group: Y <input type="checkbox"/> N <input type="checkbox"/> NR <input type="checkbox"/>	Differential loss to follow-up <10%: Y <input type="checkbox"/> N <input type="checkbox"/> NR <input type="checkbox"/>	Overall loss to follow-up <20%: Y <input type="checkbox"/> N <input type="checkbox"/> NR <input type="checkbox"/>	Reporting of specified outcomes: Y <input type="checkbox"/> N <input type="checkbox"/>
Overall quality score (use protocol for criteria): good <input type="checkbox"/> fair <input type="checkbox"/> poor <input type="checkbox"/>			

METHODS

Patient Population

Inclusion criteria:	Exclusion criteria:
Disease location:	
Definition of cohort:	
Case:	Control:

Study Interventions

- Biologic systemic agent versus nonbiologic systemic agent
- Biologic systemic agent versus phototherapy
- Class comparisons

*Multiple therapies will only be included if the common interventions are similar across groups compared and the final comparison is of a single biologic systemic agent with a single nonbiologic systemic agent or phototherapy.

<u>Intervention 1</u>	<u>Intervention 2</u>	<u>Intervention 3</u>	<u>Intervention 4</u>
Pharmacologic Class:	Pharmacologic Class:	Phototherapy:	Pharmacologic Class:
Drug name:	Drug name:	Name:	Drug name:
Dose:	Dose:	Description of the regimen (exact):	Dose:
Route:	Route:		Route:
Frequency:	Frequency:		Frequency:
Timing of first dose:	Timing of first dose:		Timing of first dose:
Duration of therapy (no. days):			
Other (drug holiday, regimen details):			
Concurrent medications:		Concurrent topical agents:	

Characteristic	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Comments
Number of participants (N)					
Age, years (mean±SD, median IQR)					
Female n/N (%)					
Race n/N (%)					
• White					
• Black					
• Asian					
• Other					
Hispanic					
Weight, kg (mean ± SD, range)					
BMI (mean ± SD, range)					
Smoker n/N (%)					
Obesity n/N (%)					
Lipids (mean ± SD)					
• LDL					
• HDL					
• Total Cholesterol					
• TG					
HRQoL(mean ± SD)					
• DLQI					
• HAQ-DI					
• EQ-5D IS					
• EQ-5D VAS					

Baseline disease severity					
<ul style="list-style-type: none"> • PASI (mean \pm SD, range) • % 					
<ul style="list-style-type: none"> • BSA (%) 					
<ul style="list-style-type: none"> • PGA (%) Moderate 					
Moderate to severe					
Very severe					
Concomitant psoriatic arthritis n/N (%)					
Disease duration, years (mean \pm SD, range)					
Neutralizing antibodies n/N (%)					
Naïve to psoriasis therapy (specify) n/N (%)					
No. patients previously treated n/N (%)					
No. previous treatments					
<ul style="list-style-type: none"> • 0 • 1 					
<ul style="list-style-type: none"> • 2-3 					
<ul style="list-style-type: none"> • >3 					
Previous treatment failure n/N (%)					
Compliance (mean \pm SD)					
Dose (mean \pm SD)					

Final health Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary estimate	Variances
Total Mortality n/N (%)						
• DLQI						
• HAQ-DI						
• EQ-5D						
• EQ-5D						
MACE						
Diabetes n/N (%)						
Psychological comorbidities						
• Depression n/N (%)						
• Suicide n/N (%)						

Intermediate Health Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary Estimate	Variances
BSA (mean \pm SD, range)						
PASI (mean \pm SD)						

Intermediate Health Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary Estimate	Variances
PASI						
PASI n/N (%)						
• PASI 50						
• PASI 75						
• PASI 90						
• PASI 100						
Physician's Global Assessment (PGA) "clear" or "minimal"						

Intermediate Health Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary Estimate	Variations
Mean Physician's Global Assessment (PGA)						
Symptom Improvement n/N (%)						
Patient's assessment of global improvement (PaGA)						

Adverse Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary Estimate	Variations
Hepatotoxicity						
• AST n/N (%)						
• ALT n/N (%)						
Nephrotoxicity						
• SCr or GFR						

Adverse Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary Estimate	Variance
Hematologic Toxicity						
• Thrombocytopenia n/N (%)						
• Anemia n/N (%)						
• Neutropenia n/N (%)						
Hypertension n/N (%)						
Metabolic alterations						
• Glucose (mean ± SD)						
• HDL (mean ± SD)						
• LDL (mean ± SD)						
• Total Cholesterol (mean ± SD)						
• TG (mean ± SD)						
• BMI (mean ± SD)						
• Thyroid function n/N (%)						
Injection site reaction n/N (%)						
Malignancy						
Infections n/N (%)						
Study Withdrawal n/N (%)						

Adverse Outcomes						
Outcome	Definition	Time point	Intervention 1	Intervention 2	Summary Estimate	Variations
Study Withdrawal due to study drug n/N (%)						

Does this trial or study have sub group analysis looking at age, gender, race, weight, smoking status, psoriasis severity, presence or absence of concomitant psoriatic arthritis, disease duration, baseline disease severity, affected BSA, disease location, number and type of previous treatments, failure of previous treatments or presence of neutralizing antibodies? Yes No If yes, report data:

Does this trial or study have information that might be used to answer?

KQ1? Yes No Class comparisons? Yes

KQ2? Yes No Class comparisons? Yes

KQ3? Yes No Class comparisons? Yes

If yes, please print a copy of the article and put into the correct pile for KQ1, 2 or 3.

Appendix C. Excluded Studies from Full-Text Review

Table 1. Excluded studies at the full text level from primary search

Excluded because citation was not a full text systematic review, study or trial (n=50)
Ahmad K, McDonnell TJ, Rogers S. Does prior treatment with fumaric acid esters predispose to tuberculosis in patients on etanercept? <i>Clin Exp Dermatol</i> 2007;32:329.
Amital H, Ingber A, Rubinow A. Infliximab-induced remission of extensive plaque psoriasis. <i>Isr med Assoc J</i> 2003;5:827-28.
Balato N, Gallo L, Gaudiello F, et al. Transient and reversible thrombocytopenia in a psoriatic patient treated with etanercept. <i>J Dermatolog Treat</i> 2010;21:117-18.
Bansal C, Leonardi C, Van Voorhees AS. Persistent CD4+ T cell depression following combination alefacept and methotrexate therapy. <i>Int J Dermatol</i> 2008;47:1204-06.
Barland C, Kerdel FA. Addition of low-dose methotrexate to infliximab in the treatment of a patient with severe, recalcitrant pustular psoriasis. <i>Arch Dermatol</i> 2003;139:949-50.
Berns MW, McCullough JL. Porphyrin sensitized phototherapy. <i>Arch Dermatol</i> 1986;122:871-74.
Carrascosa J M, Soria X, Ferrandiz C. Effective management of a psoriatic flare with narrowband UVB phototherapy during efalizumab therapy without discontinuing treatment. <i>J Eur Acad Dermatol Venereol</i> 2007;21:828-29.
Dalaker M, Bonesronning JH. [Treatment of severe psoriasis with anti-TNF-alpha-antibody and methotrexate]. <i>Tidsskr Nor Laegeforen</i> 2003;123:1070-71.
Daulat S, Detweiler JG, Pandya AG. Development of pemphigus vulgaris in a patient with psoriasis treated with etanercept. <i>J Eur Acad Dermatol Venereol</i> 2009;23:483-84.
Davison SC, Bunker CB, Basarab T. Etanercept for severe psoriasis and psoriatic arthritis: observations on combination therapy. <i>Br J Dermatol</i> 2002;147:831-32.
Dawe RS. Using 'number needed to treat' to express the magnitudes of benefit of ultraviolet B phototherapy and of antitumour necrosis factor-alpha therapies for psoriasis. <i>Br J Dermatol</i> 2010;162:456-57.
Drijkoningen M, De Wolf-Peeters C, Roelandts R, et al. A morphological and immunohistochemical study of phytophotodermatitis-like bullae induced by PUVA. <i>Photodermatol</i> 1986;3:199-201.
Dubin DB, Tanner W, Ellis R. Biologics for psoriasis. <i>Nat Rev Drug Discov</i> 2003;2:855-56.
Egnatios G, Warthan MM, Pariser R, et al. Pustular psoriasis following treatment of rheumatoid arthritis with TNF-alpha inhibitors. <i>J Drugs Dermatol</i> 2008;7:975-77.
Elewski BE. Infliximab for the treatment of severe pustular psoriasis. <i>J Am Acad Dermatol</i> 2002;47:796-97.
Fiala K, Schierl M, Breier F, et al. Transient paresis of the right recurrent laryngeal nerve after treatment with etanercept for plaque-type psoriasis. <i>Eur J Dermatol</i> 2010;20:818-19.
Gonzalo-Garijo MA, Perez-Calderon R, de Argila Fernandez-Duran D. Severe generalized exanthema due to etanercept given for severe plaque psoriasis. <i>Ann Allergy Asthma Immunol</i> 2008;100:621-22.
Gonzalo-Garijo M A, Rodriguez-Nevado I, Perez-Calderon R, et al. Severe cutaneous reaction and fever due to adalimumab. <i>Ann Allergy Asthma Immunol</i> 2010;105:490-91.
Heikkila H, Ranki A, Cajanus S, et al. Infliximab combined with methotrexate as long-term treatment for erythrodermic psoriasis. <i>Arch Dermatol</i> 2005;141:1607-10.
Jackle R. [Vitamin D3 analogs, oral fumaric acid, TNF-alpha antibodies. New hope for patients with psoriasis]. <i>MMW Fortschr Med</i> 2001;143:4-8.
Katz KA. Psoriasis Area and Severity Index 50 as an endpoint in psoriasis trials: an unconvincing proposal. <i>J Am Acad Dermatol</i> 2005;53:547-51.
Kincaid L. Psoriasis: TNF-alpha inhibitors and beyond. <i>Drug Discov Today</i> 2005;10:884-86.
Kluger N, Girard C, Guillot B, et al. Efficiency and safety of etanercept after acute hepatitis induced by infliximab for psoriasis. <i>Acta Derm Venereol</i> 2009;89:332-34.
Lee MR, Cooper AJ. Use of infliximab in the treatment of psoriasis. <i>Australas J Dermatol</i> 2004;45:193-95.
Lucas A, Belinchon I, Perez-Crespo M, et al. Successful response to narrow-band UVB in a patient undergoing concomitant treatment with adalimumab for psoriasis. <i>Australas J Dermatol</i> 2008;49:173-74.
McCluggage LK, Hussar DA. New drugs: Ustekinumab, tocilizumab, and telavancin hydrochloride. <i>J Am Pharm Assoc</i> 2010;50:324-27.
Menter A. Goeckerman therapy versus biologics in the treatment of psoriasis. <i>J Am Acad Dermatol</i> 2010;62:516-17.
Mocciaro F, Renna S, Orlando A, et al. Severe cutaneous psoriasis after certolizumab pegol treatment: report of a case. <i>Am J Gastroenterol</i> 2009;104:2867-68.
Mrowietz U, Barth J, Boehncke WH, et al. [Therapy of psoriasis vulgaris and psoriatic arthritis with etanercept]. <i>J Deutschen Dermatologischen Gesellschaft</i> 2005;3:470-72.
Naidoo P, Rambiritch V. Voclosporin (ISA247) for plaque psoriasis. <i>Lancet</i> 2008;372:888-89.

Nakagomi D, Harada K, Yagasaki A, et al. Psoriasiform eruption associated with alopecia areata during infliximab therapy. *Clin Exp Dermatol* 2009;34:923-24.

Naldi L. The search for effective and safe disease control in psoriasis. *Lancet* 2008;371:1311-12.

Nijsten T, Spuls PI. Adalimumab may be better or no worse than methotrexate in the treatment of psoriasis. *Br J Dermatol* 2008;159:257-58.

Nikkels AF, Pierard GE. Etanercept and recalcitrant acrodermatitis continua of Hallopeau. *J Drugs Dermatol* 2006;5:705-06.

Olivieri I, D'Angelo S, Leccese P, et al. Worsening of psoriasis with rituximab therapy. *Clin Exp Rheumatol* 2010;28:926.

Ozdemir M, Mevlitoglu I, Balevi A. Acitretin narrow-band TL-01 phototherapy but not etanercept treatment improves a localized inflammatory linear verrucous epidermal naevus with concomitant psoriasis. *J Eur Acad Dermatol Venereol* 2009;23:1453-54.

Papadavid E, Makris M, Dalamaga M, et al. Recall injection-site reactions to etanercept in a patient with psoriasis. *Clin Exp Dermatol* 2009;34:414-15.

Pereira TM, Vieira AP, Fernandes JC, et al. Anti-TNF-alpha therapy in childhood pustular psoriasis. *Dermatology* 2006;213:350-52.

Rallis E, Verros CD. Ustekinumab treats psoriasis refractory to seven conventional and biologic therapies. *Dermatol Online J* 2011;17:14.

Renner R, Colman A, Sticherling M. ILVEN: is it psoriasis? Debate based on successful treatment with etanercept. *Acta Derm Venereol* 2008;88:631-32.

Rokhsar C, Rabhan N, Cohen SR. Etanercept monotherapy for a patient with psoriasis, psoriatic arthritis, and concomitant hepatitis C infection. *J Am Acad Dermatol* 2006;54:361-62.

Strober BE. Successful treatment of psoriasis and psoriatic arthritis with etanercept and methotrexate in a patient newly unresponsive to infliximab. *Arch Dermatol* 2004;140:366.

Taniguchi Y, Kumon Y, Shimamura Y, et al. Rapidly progressive destructive arthritis in psoriatic arthritis sine psoriasis: do bone resorption marker levels predict outcome of bone destruction in psoriatic arthritis? *Mod Rheumatol* 2011;21:106-108.

Thielen AM, Barde C, Saurat JH. Infliximab- and methotrexate-resistant rebound of psoriasis after discontinuation of efalizumab (Raptiva). *Br J Dermatol* 2006;155:846-47.

Tuxen AJ, Yong MK, Street AC, et al. Disseminated cryptococcal infection in a patient with severe psoriasis treated with efalizumab, methotrexate and ciclosporin. *Br J Dermatol* 2007;157:1067-68.

Ventura F, Gomes J, Duarte Mda L, et al. Efficacy and safety of etanercept in patients with psoriasis and hepatitis C. *Eur J Dermatol* 2010;20:808-09.

Warren RB, Brown BC, Carmichael AJ, et al. Long-term control of recalcitrant psoriasis with combination infliximab and methotrexate. *Clin Exp Dermatol* 2009;34:415-16.

Yamauchi PS, Lowe NJ. Cessation of cyclosporine therapy by treatment with etanercept in patients with severe psoriasis. *J Am Acad Dermatol* 2006;54:S135-38.

Yamauchi PS, Lowe NJ, Gindi V. Treatment of coexisting bullous pemphigoid and psoriasis with the tumor necrosis factor antagonist etanercept. *J Am Acad Dermatol* 2006;54:S121-22.

No authors listed. [Aldalimumab in psoriatic arthritis and as the initial therapy in rheumatoid arthritis]. *Krankenpfl J* 2005;43:244.

Excluded because the population was not human adults (n=1)

Sasson M, Stiller MJ, Shupack JL, et al. Antibody titers to an oxidized thymidine moiety are altered by systemic pharmacotherapy and by ultraviolet B phototherapy. *Arch Dermatol Res* 1993;285:227-29.

Excluded because the population was not patients with chronic plaque psoriasis or psoriasis vulgaris (n=10)

Bose F, Raeli L, Garutti C, et al. Dual role of anti-TNF therapy: enhancement of TCR-mediated T cell activation in peripheral blood and inhibition of inflammation in target tissues. *Clin Immunol* 2011;139:164-76.

Cassano N, Loconsole F, Amoroso A, et al. Infliximab monotherapy for refractory psoriasis: preliminary results. *Int J Immunopathol Pharmacol* 2004;17:373-80.

Kamili QU, Miner A, Hapa A, et al. Infliximab treatment for psoriasis in 120 patients on therapy for a minimum of one year: a review. *J Drugs Dermatol* 2011;10:539-44.

Mease PJ. Cytokine blockers in psoriatic arthritis. *Ann Rheum Dis* 2001;60:37-40.

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Table 2. Excluded studies at the full text level for search two

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Appendix D. Baseline Characteristics for Included Studies and Trials

Table 3. Baseline characteristics of included studies

Study, Year	Group	N	Age (y) mean(SD)	Female n/N (%)	Race/ethnic group n/N (%)	Wt (kg) mean(SD)	BMI (kg/m ²) mean(SD)	PASI mean(SD)	BSA (%) mean(SD)	Disease duration (y) mean(SD)	Psoriatic arthritis n/N (%)
Barker, 2011	Infliximab	653	44.1 (18-78)*	215/653 (32.9)	W:636/653(97.3)	84.5(18.6)	28.0(5.8)	21.4(8.0)†	31.9(16.5)†	18.8(11.6)	118/653 (18.1)
	MTX	215	41.9 (18-69)*	67/215 (31.2)	W:211/215(98.1)	83.8(18.2)	27.7(5.0)	21.1(7.6)	31.0(15.0)	17.0(10.3)	36/215 (16.7)
Inzinger, 2011‡	Biologics§	130	46.2(11.8)	61/172 (35.5)¶	---	---	---	16.9(7.3)	---	22.9(10.5)	---
	PUVA	118	48.5(15.7)	---	---	---	---	15.0(4.0)	---	23.4(11.9)	---
Strober, 2011	MTX to adalimumab	41	47.4(13.1)	13/41 (31.7)	W:39/41(95.1)	89.5(17.5)	---	10.2(5.5)	10.9(7.3)	19.8(13.5)	17/41 (41.5)
	NBUVB to adalimumab	29	45.7(14.6)	13/29 (44.8)	W:25/29(86.2)	86.0(17.8)	---	12.8(5.7)	14.5(12.6)	23.0(14.1)	7/29 (24.1)
Garavaglia, 2010	CyA to etanercept	4	58.3(12.2)	1/4 (25.0)	---	---	---	---	---	17.0(12.0)	1/4 (25.0)
Caproni, 2009	Etanercept	30	NR (28-67)**	17/30 (56.7)	---	---	---	21.5(9.1)	---	---	0/30 (0)
	Acitretin	30	NR (31-65)**	19/30 (63.3)	---	---	---	22.3(5.7)	---	---	0/30 (0)
Mazzotta, 2009‡	Nonbiologics or phototherapy to etanercept††	98	---	---	---	---	---	16.1(7.1)	---	---	---
Gisondi, 2008a	Etanercept	22	55.3(10.9)	10/22 (45.4)	---	79.5(9.4)	27.3(6.0)	11.0(4.6)	12.6(6.3)	23.5(10.9)	0/22 (0)
	Acitretin	20	55.0(11.3)	8/20 (40.0)	---	78.4(10.3)	27.2(3.1)	10.4(5.3)	11.1(7.3)	18.8(16.6)	0/20 (0)
Gisondi, 2008b	Etanercept	58	50.2(11.1)	19/58 (32.7)	---	80.1(16.2)	27.6(5.0)	18.8(7.4)	---	22.0(12.9)	0/58 (0)
	Infliximab	40	46.8(11.2)	12/40 (30.0)	---	79.2(15.2)	26.5(3.5)	17.7(7.3)	---	17.5(13.4)	0/40 (0)
	MTX	43	53.1(12.7)	17/43 (39.5)	---	81.0(12.6)	27.4(3.6)	8.2(3.1)	---	18.6(12.0)	0/43 (0)

Study, Year	Group	N	Age (y) mean(SD)	Female n/N (%)	Race/ethnic group n/N (%)	Wt (kg) mean(SD)	BMI (kg/m ²) mean(SD)	PASI mean(SD)	BSA (%) mean(SD)	Disease duration (y) mean(SD)	Psoriatic arthritis n/N (%)
Saurat, 2008	Adalimumab	108	42.9(12.6)	38/108 (35.2)	W:98/103(95.1) B:2/103(1.9) A:3/103(2.9) O:0/103(0) H:11/103(10.7)	81.7(20.0)	---	20.2(7.5)	33.6(19.9)	17.9(10.1)	23/108 (21.3)
	MTX	110	41.6(12.0)	37/110 (33.6)	W:103/108(95.4) B:1/108(0.9) A:4/108(3.7) O:0/108(0) H:9/108(8.3)	83.1(17.5)	---	19.4(7.4)	32.4(20.6)	18.9(10.2)	19/110 (17.3)
	MTX to adalimumab	95	---	---	---	---	---	---	---	---	---
Magliocco, 2007	CyA to alefacept	11	45 (25-65)††	---	---	---	---	---	---	22(7-32)*	---
Costanzo, 2005‡	Nonbiologics to etanercept§§	44	41.2(NR)	16/44 (36.4)	---	---	---	15.6(NR)	21.7(NR)	15.5(NR)	15/44 (34.1)

Table note: A=asian; B=black; BMI=body mass index; BSA=body surface area; CyA=cyclosporine; d=day(s); H=hispanic; kg=kilogram(s); m=meter(s); MTX=methotrexate; N=total population; NBUVB=narrowband ultraviolet B; NR=not reported; O=other; PASI=Psoriasis Area and Severity Index; PUVA=psoralen plus ultraviolet A; SD=standard deviation; W=white; Wt=weight; y=year(s); ---=not reported

* Mean(range)

† n=650

‡ Baseline characteristics reported by drug class, not individual agent

§ Adalimumab, alefacept, etanercept, infliximab, ustekinumab

|| Number corresponds to treatment courses, not patients

¶ Total population, n=172

** Median(range)

†† CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

‡‡ Mean(Interquartile range)

§§ CyA, corticosteroids, MTX, retinoids

Appendix E. Quality and Characteristics of Included Trials and Studies

Table 4. Characteristics and quality assessment of included studies

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Barker, 2011 RESTORE1	<p>Publication type: Full text, manuscript before edit, clinical trial registry</p> <p>Study design: RCT with optional transition period</p> <p>Geographic location: Europe</p> <p>Funding: Industry</p> <p>Conflict of interest reported? Yes</p> <p>Number of centers: 106</p> <p>Randomization and allocation concealment: At each eligible subject's baseline visit, study centers phoned the Interactive Voice Response System (IVRS; Quintiles, Morrisville, North Carolina, USA) for randomization. IVRS assigned a patient randomization number. Patients were randomized 3:1 to receive infliximab:MTX</p> <p>Outcome assessment: Patients were assessed for clinical response at all visits.</p> <p>Total number randomized: 868 (868)</p>	<p>Inclusion criteria: Patients 18y to 75y diagnosed with moderate to severe plaque psoriasis for ≥6 months prior to screening, candidates for phototherapy or systemic treatment, and BSA ≥10% involvement and PASI ≥12</p> <p>Exclusion criteria: Previous treatment with MTX, or with a biologic or TNF antagonist within 3 months of baseline; diagnosis of CHF, history of chronic or recurrent infectious disease, or serious infection, or had been hospitalized or received IV antibiotics for infection within past 2 months; opportunistic infection within past 6 months; history or signs/ symptoms of lymphoproliferative disease; active or history of malignancy</p> <p>Intervention 1: Infliximab 5mg/kg IV infusion at weeks 0, 2, 6, 14, 22</p> <p>Intervention 2: MTX 15mg PO per week for 22 weeks</p>	<p>Duration of followup: 26 weeks</p> <p>Followup: Infliximab 100% MTX 100%</p> <p>Final outcomes: HRQoL (DLQI, EQ-5D), SF36</p> <p>Intermediate outcomes: PASI, PGA, individual symptom improvement (pruritus)</p> <p>Adverse events: Hepatotoxicity (LFT abnormalities), injection site reaction, malignancy, infection, study withdrawal</p>	<ol style="list-style-type: none"> 1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to intervention status? NR 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Was incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups < 10%? Yes 10. Was the overall loss to followup < 20%? Yes <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Inzinger, 2011	<p>Publication type: Full text, Abstract</p> <p>Study design: Observational, Cohort study</p> <p>Geographic location: Austria</p> <p>Funding: Industry</p> <p>Conflict of interest reported? Yes</p> <p>Number of centers: 1</p> <p>Outcome assessment: Data on patient characteristics and clinical PASI reduction categories were extracted from the electronic databank of the Psoriasis Registry, Graz</p> <p>Confounders adjusted for: As patients underwent more than one treatment cycle, scores from individual treatments were not independent and the test had to be adapted</p> <p>Total number studied: 248 (199)[†]</p>	<p>Inclusion criteria: Patients ≥18y with chronic plaque psoriasis treated with oral PUVA and/or at least one course of a biologic agent</p> <p>Exclusion criteria: NR</p> <p>Definition of cohort: Patients with psoriasis treated regularly with PUVA vs. biologics under daily life conditions outside of clinical trials between January 2003 and February 2010</p> <p>Intervention 1: Biologics (adalimumab; alefacept; etanercept; infliximab; ustekinumab; standard therapy for all except median dose of etanercept 25mg SC twice a week)</p> <p>Intervention 2: 8-MOP plus UVA 2 to 4 times per week for a minimum of 3 months</p>	<p>Duration of followup: Biologics 12 weeks PUVA 8-MOP 10.3 weeks (median)</p> <p>Followup: Biologics[§] 100% Phototherapy 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: PASI</p> <p>Adverse events: NR</p>	<ol style="list-style-type: none"> 1. Was the selection of cohorts unbiased? Yes 2. Were the groups selected to minimize baseline differences? Yes 3. Was the description of the cohort adequate? Yes 4. Was the selection of a comparison group adequate? Yes 5. Was the sample size calculated? NR 6. Were outcome assessments blinded? NR 7. Were outcomes assessed using a valid methodology? Yes 8. Was intention to treat analysis used? Yes 9. Was adequate control for confounding used in the analysis? Partially 10. Was the differential loss to followup between the compared groups < 10%? Yes 11. Was the overall loss to followup < 20%? Yes <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Strober, 2011	<p>Publication type: Full text, Abstract, ClinicalTrials.gov results</p> <p>Study design: Observational, Cohort study</p> <p>Geographic location: United States and Canada</p> <p>Funding: Industry</p> <p>Conflict of interest reported? Yes</p> <p>Number of centers: 24</p> <p>Outcome assessment: PGA, PASI, DLQI and a VAS for plaque psoriasis and PsA pain were measured at each visit</p> <p>Total number studied: 152 (70)</p>	<p>Inclusion criteria: Age ≥18y; chronic plaque psoriasis ≥6 months; suboptimal response to prior therapy with etanercept, MTX, or NBUVB phototherapy; patients achieving a PGA of "mild" or worse after ≥4 months MTX therapy or a PGA of "moderate" or worse after ≥2 months NBUVB therapy at screening; patients with latent TB were permitted if prophylactic treatment was initiated before administration of study drug; women of childbearing potential were required to use contraception</p> <p>Exclusion criteria: Prior treatment with adalimumab or natalizumab; concurrent active skin diseases or infections; history of neurologic symptoms suggestive of CNS demyelinating disease; history of cancer or lymphoproliferative disease other than successfully treated nonmelanoma skin cancer or localized carcinoma in situ of the cervix</p> <p>Definition of cohort: Patients enrolled between December 28, 2008 and April 14, 2009</p> <p>Interventions: Patients failing MTX or NBUVB were transitioned to adalimumab 80mg SC at week 0, then 40mg SC every other week for weeks 1 to 15, after washout period of 4-10 days</p>	<p>Duration of followup: 70 days after end of adalimumab treatment (16 weeks + 70 days)</p> <p>Followup: MTX transitioned to adalimumab 100% NBUVB transitioned to adalimumab 100%</p> <p>Final outcomes: Mortality, HRQoL (DLQI)</p> <p>Intermediate outcomes: PASI, PGA, Individual symptom improvement (Pain involving Psoriatic Plaques and/or PsA, Psoriasis-related Pruritus Assessment)</p> <p>Adverse events: Metabolic alterations (TG), injection site reaction, malignancy, infection, study withdrawal</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? No</p> <p>4. Were outcome assessors blind to intervention status? NR</p> <p>5. Were the methods used for randomization adequate? NA</p> <p>6. Were methods for allocation concealment adequate? NA</p> <p>7. Was incomplete outcome data adequately addressed? Yes</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? No</p> <p>10. Was the overall loss to followup < 20%? Yes</p> <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Garavaglia, 2010	<p>Publication type: Full text</p> <p>Study design: Observational, Cohort study</p> <p>Geographic location: Italy</p> <p>Funding: NR</p> <p>Conflict of interest reported? NR</p> <p>Number of centers: 1</p> <p>Outcome assessment: AST, ALT, viral load and PASI were monitored at 3-month intervals from the start of treatment up to two years after the initiation of etanercept therapy</p> <p>Total number studied: 5 (4)</p>	<p>Inclusion criteria: Diagnosis of psoriasis and/or psoriatic arthritis; positive HCV status as determined by serological testing for anti-HCV antibodies; active etanercept therapy</p> <p>Exclusion criteria: NR</p> <p>Definition of cohort: Patients attending the dermatology service of the Istituto Galeazzi, Milan, between 2007 and 2009</p> <p>Intervention: Patients previously treated with CyA (dose/route/frequency NR) were treated with etanercept 50mg per week</p>	<p>Duration of followup: 2 years</p> <p>Followup: CyA transitioned to etanercept 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: PASI</p> <p>Adverse events: Hepatotoxicity (AST, ALT)</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? NA</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? No</p> <p>4. Were outcome assessors blind to intervention status? NR</p> <p>5. Were the methods used for randomization adequate? NA</p> <p>6. Were methods for allocation concealment adequate? NA</p> <p>7. Was incomplete outcome data adequately addressed? Yes</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? Yes</p> <p>10. Was the overall loss to followup < 20%? Yes</p> <p>Overall quality rating: Poor</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Caproni, 2009	<p>Publication type: Full text, Abstract</p> <p>Study design: RCT</p> <p>Geographic location: Italy</p> <p>Funding: NR</p> <p>Conflict of interest reported? NR</p> <p>Number of centers: NR</p> <p>Randomization and allocation concealment: Patients randomly assigned to one of the two groups, etanercept or acitretin</p> <p>Outcome assessment: At the baseline and at the end of the treatment, a blind clinical assessment by calculating PASI was made, and blood samples were taken to evaluate IL-17, IL-22 and IL-23 levels</p> <p>Total number randomized: 60 (60)</p>	<p>Inclusion criteria: Moderate to severe plaque-type psoriasis without joint involvement defined as BSA \geq10% involvement and PASI \geq 10</p> <p>Exclusion criteria: Patients treated in the previous month with any topical or systemic psoriasis therapy; history or risk of serious infection, lymphoproliferative disease or active or latent TB</p> <p>Intervention 1: Etanercept 50mg twice a week for 12 weeks</p> <p>Intervention 2: Acitretin 0.4mg/kg/d for 12 weeks</p>	<p>Duration of followup: 12 weeks</p> <p>Followup: Etanercept 100% Acitretin 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: PASI</p> <p>Adverse events: Study withdrawal</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? NR</p> <p>4. Were outcome assessors blind to intervention status? Yes</p> <p>5. Were the methods used for randomization adequate? NR</p> <p>6. Were methods for allocation concealment adequate? NR</p> <p>7. Was incomplete outcome data adequately addressed? Yes</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? Yes</p> <p>10. Was the overall loss to followup < 20%? Yes</p> <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Mazzotta, 2009	<p>Publication type: Full text</p> <p>Study design: Observational-class level data only, Cohort study</p> <p>Geographic location: Italy</p> <p>Funding: Not funded</p> <p>Conflict of interest reported? Yes</p> <p>Number of centers: 1</p> <p>Outcome assessment: Clinical and laboratory evaluations were performed at baseline (week 0) and after 12 and 24 weeks of treatment</p> <p>Confounders adjusted for: NA</p> <p>Total number randomized: 234 (124)</p>	<p>Inclusion criteria: Patients 18 – 80y affected by moderate to severe plaque-type psoriasis or psoriatic arthritis who had had an unsatisfactory clinical response or resistance to traditional or biologic systemic treatments</p> <p>Exclusion criteria: Subjects with co-morbid conditions that were contraindications to anti-TNF treatment</p> <p>Definition of cohort: Patients were recruited from an academic dermatology outpatient clinic, during the period from May 2004 to April 2005</p> <p>Intervention: Nonbiologics (CyA, retinoids, corticosteroids, MTX, fumaric acid esters) or phototherapy (PUVA) transitioned to etanercept 50mg SC twice weekly for 12 weeks then reduced to 25mg SC twice weekly for 12 weeks</p>	<p>Duration of followup: 24 weeks</p> <p>Followup: Nonbiologics or phototherapy transitioned to etanercept¶ 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: PASI</p> <p>Adverse events: NR</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? NA</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? NA</p> <p>4. Were outcome assessors blind to intervention status? NR</p> <p>5. Were the methods used for randomization adequate? NA</p> <p>6. Were methods for allocation concealment adequate? NA</p> <p>7. Was incomplete outcome data adequately addressed? Yes</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? Yes</p> <p>10. Was the overall loss to followup < 20%? Yes</p> <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Gisondi, 2008a	<p>Publication type: Full text, Abstract</p> <p>Study design: RCT</p> <p>Geographic location: Italy</p> <p>Funding: NR</p> <p>Conflict of interest reported? NR</p> <p>Number of centers: 1</p> <p>Randomization and allocation concealment: Randomization was performed with the use of computer-generated random numbers and block size of four patients</p> <p>Outcome assessment: The PASI assessor was blinded concerning the group allocation of the patient</p> <p>Total number randomized: 60 (42)</p>	<p>Inclusion criteria: Patient ≥ 18y with active, stable moderate to severe plaque psoriasis</p> <p>Exclusion criteria: Diagnosis of PsA or other type of psoriasis (gutatte, erythrodermic, or pustular); active or chronic infections(HIV, HBV, HCV, latent TB); previous or active malignancies except for skin carcinomas; severe hematological, renal and hepatic disorders that could contraindicate acitretin and /or etanercept; severe CHF; demyelinating diseases; fertile women; elevation of serum cholesterol > 4.90 mmol/ L (220 mg/dL) and serum triglycerides > 1.70 mmol/ L (180 mg/dL); previous treatment with biologics; and receipt of phototherapy or any systemic or topical therapy for psoriasis within the previous 4 weeks.</p> <p>Intervention 1: Etanercept 25mg SC twice weekly</p> <p>Intervention 2: Acitretin 0.4mg/kg/d PO</p>	<p>Duration of followup: 24 weeks</p> <p>Followup: Etanercept 100% Acitretin 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: BSA, PASI</p> <p>Adverse events: Hepatotoxicity (AST and ALT), metabolic alterations (TC, TG), study withdrawal</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? Partially</p> <p>4. Were outcome assessors blind to intervention status? Yes</p> <p>5. Were the methods used for randomization adequate? Yes</p> <p>6. Were methods for allocation concealment adequate? Yes</p> <p>7. Was incomplete outcome data adequately addressed? Yes</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? Yes</p> <p>10. Was the overall loss to followup < 20%? Yes</p> <p>Overall quality rating: Good</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Gisondi, 2008b	<p>Publication type: Full text</p> <p>Study design: Observational, Cohort study</p> <p>Geographic location: Italy</p> <p>Funding: NR</p> <p>Conflict of interest reported? NR</p> <p>Number of centers: 1</p> <p>Outcome assessment: All subjects were visited by a dermatologist who registered demographical, biometrical and the other relevant data on a case report form. Relevant data collected included age, gender, weight, height, body mass index (BMI), age of psoriasis onset, type and severity of psoriasis and concomitant medications</p> <p>Confounders adjusted for: NR</p> <p>Total number studied: 141 (141)</p>	<p>Inclusion criteria: Patients with diagnosis of chronic plaque psoriasis according to clinical criteria; resistant or intolerant to MTX</p> <p>Exclusion criteria: Patients with psoriatic arthritis diagnosed according to the CASPAR criteria</p> <p>Definition of cohort: Patients consecutively admitted to the outpatient clinics of the University Hospital of Verona were involved. The source population of the study was people living in city of Verona or in the neighborhood</p> <p>Intervention 1: Etanercept 25mg SC twice a week for 6 months</p> <p>Intervention 2: Infliximab 5mg/kg IV at week 0, 2, 6 and every 8 weeks for 6 months</p> <p>Intervention 3: MTX 15mg IM once a week for 6 months</p>	<p>Duration of followup: 6 months</p> <p>Followup: Etanercept 100% Infliximab 100% MTX 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: PASI</p> <p>Adverse events: Metabolic alterations (TC, TG, BMI, weight)</p>	<ol style="list-style-type: none"> 1. Was the selection of cohorts unbiased? Yes 2. Were the groups selected to minimize baseline differences? Yes 3. Was the description of the cohort adequate? Yes 4. Was the selection of a comparison group adequate? Yes 5. Was the sample size calculated? NR 6. Were outcome assessments blinded? NR 7. Were outcomes assessed using a valid methodology? Yes 8. Was intention to treat analysis used? Yes 9. Was adequate control for confounding used in the analysis? NR 10. Was the differential loss to followup between the compared groups < 10%? Yes 11. Was the overall loss to followup < 20%? Yes <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Saurat, 2008 CHAMPION	<p>Publication type: Full text, abstract</p> <p>Study design: RCT with OLE</p> <p>Geographic location: Europe and Canada</p> <p>Funding: Industry</p> <p>Conflict of interest reported? Yes</p> <p>Number of centers: 28</p> <p>Randomization and allocation concealment: Randomized through a central computer-generated scheme stratified by center, with block sizes of four. Patient numbers were centrally assigned by an interactive voice-response system in consecutive order in a 2:2:1 ratio (Adalimumab:MTX:placebo)</p> <p>Outcome assessment: A qualified investigator from each site performed clinical efficacy assessments at each study visit and remained throughout the study, if possible</p> <p>Total number randomized: 271 (218)</p>	<p>Inclusion criteria: Age ≥18y; moderate to severe psoriasis defined as BSA ≥10% involvement and PASI ≥ 10; plaque psoriasis ≥1 year; stable ≥2 months; candidates for systemic therapy or phototherapy with active psoriasis despite topical treatments; naïve to both TNF-antagonists and MTX; patients with latent TB were permitted if prophylactic treatment was initiated before administration of study drug; all men and women of childbearing potential were required to use contraception; patients must have been willing to self-administer SC injections or have a qualified person administer them</p> <p>Exclusion criteria: A history of clinically significant hematological, renal or liver disease /abnormal laboratory values; history of demyelinating disease, cancer, or other lymphoproliferative disease (other than successfully treated nonmetastatic cutaneous squamous cell or basal cell carcinoma and/or localized carcinoma in situ of the cervix); immunocompromised patients</p> <p>RCT intervention 1: Adalimumab 80mg SC at week 0, then 40mg SC every other week for weeks 1 to 15</p> <p>RCT intervention 2: MTX 7.5mg PO weekly, increased as needed and tolerated to 25mg weekly†</p> <p>OLE study: Patients on MTX were transitioned to adalimumab 40mg SC every other week</p>	<p>Duration of followup: 70 days after last treatment (16 weeks + 70 days)</p> <p>Followup: Adalimumab100% MTX 100% OLE 100%</p> <p>Final outcomes: Mortality, HRQoL (DLQI, EQ-5D)</p> <p>Intermediate outcomes: PASI, PGA, Patient's Assessment of Global improvement, Individual symptom improvement (Pain Involving Psoriatic Plaques and/or PsA, Psoriasis-related Pruritus Assessment)</p> <p>Adverse events: Hepatotoxicity (AST, ALT), infection, study withdrawal</p>	<ol style="list-style-type: none"> 1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Was incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups < 10%? Yes 10. Was the overall loss to followup < 20%? Yes <p>Overall quality rating: Good</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Magliocco, 2007	<p>Publication type: Full text, Abstract</p> <p>Study design: Observational, Cohort study</p> <p>Geographic location: United States</p> <p>Funding: Industry</p> <p>Conflict of interest reported? Yes</p> <p>Number of centers: 1</p> <p>Outcome assessment: Efficacy assessments included PGA and the DLQI, which were measured monthly during the study. Safety assessments included monthly hematology and blood chemistry assessments while patients were on cyclosporine, CD4+ T cell monitoring weekly during alefacept treatment and monthly during the observation periods in phases II and III, and adverse event monitoring throughout the study</p> <p>Total number studied: 12 (11)</p>	<p>Inclusion criteria: Patients 18 to 80y with chronic plaque psoriasis well-controlled on cyclosporine (defined as PGA of "mild", "almost clear", or "clear"), and a need or desire to transition to alefacept therapy; required to have CD4+ T cell counts >400 cells/mm at time of enrollment</p> <p>Exclusion criteria: Pregnant or lactating; active infection (with the exception of common colds); history of HIV, HBV, HCV, heart disease, or liver disease</p> <p>Disease location: NR</p> <p>Intervention: Patients were transitioned to alefacept following three phases. Phase I (wk 1 to 12): Alefacept 15 mg IM once weekly plus CyA taper Phase II (wk 13 to 24): Neither alefacept nor CyA and only topical agents and UVB were permitted Phase III (wk 25 to 48): Alefacept 15 mg IM once weekly for the first 12 weeks then observation during the second 12 weeks where only UVB and topical therapies were permitted</p>	<p>Duration of followup: 48 weeks</p> <p>Followup: CyA transitioned to alefacept 54.5%</p> <p>Final outcomes: HRQoL (DLQI)</p> <p>Intermediate outcomes: PGA</p> <p>Adverse events: Malignancy, infection, study withdrawal</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? NA</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? No</p> <p>4. Were outcome assessors blind to intervention status? NR</p> <p>5. Were the methods used for randomization adequate? NA</p> <p>6. Were methods for allocation concealment adequate? NA</p> <p>7. Was incomplete outcome data adequately addressed? Yes</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? NA</p> <p>10. Was the overall loss to followup < 20%? No</p> <p>Overall quality rating: Fair</p>

Study, year	Trial characteristics	Population and interventions	Followup and outcomes of interest (Timing)	Quality assessment
Costanzo, 2005	<p>Publication type: Full text</p> <p>Study design: Observational, class level data only, Cohort study</p> <p>Geographic location: Italy</p> <p>Funding: NR</p> <p>Conflict of interest reported? NR</p> <p>Number of centers: NR</p> <p>Outcome assessment: Clinical and laboratory assessments were done at screening, at baseline and every 4 weeks thereafter</p> <p>Total number randomized: 44 (44)</p>	<p>Inclusion criteria: Patients 18 to 75y with chronic plaque psoriasis or psoriatic arthritis, PASI >10, and had failed at least one systemic therapy for lack of efficacy or adverse events</p> <p>Exclusion criteria: NR</p> <p>Disease location: NR</p> <p>Intervention 1: Systemic corticosteroids, CyA, MTX or retinoids transitioned to etanercept 25mg SC twice weekly</p>	<p>Duration of followup: 24 weeks</p> <p>Followup: Nonbiologics transitioned to etanercept** 100%</p> <p>Final outcomes: NR</p> <p>Intermediate outcomes: PASI</p> <p>Adverse events: Hematologic toxicity, injection site reaction, infection, study withdrawal</p>	<p>1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? NA</p> <p>2. Were outcomes assessed using a valid methodology and criteria? Yes</p> <p>3. Were subjects and providers blind to the intervention status of participants? No</p> <p>4. Were outcome assessors blind to intervention status? No</p> <p>5. Were the methods used for randomization adequate? NA</p> <p>6. Were methods for allocation concealment adequate? NA</p> <p>7. Was incomplete outcome data adequately addressed? NR</p> <p>8. Was intention to treat analysis used? Yes</p> <p>9. Was the differential loss to followup between the compared groups < 10%? Yes</p> <p>10. Was the overall loss to followup < 20%? Yes</p> <p style="text-align: right;">Overall quality rating: Fair</p>

* Duration of followup is reported as the original study's longest reported followup for outcomes of interest and followup percent is reported for the study's pre-specified primary outcome

† Total number of treatment courses

‡ Oral methotrexate was administered as a single weekly dose and was initiated at 7.5 mg per week at week 0, increased to 10 mg per week at week 2, and increased to 15 mg per week at week 4 for all patients. At week 8 onward, patients who achieved at least a 50% reduction in Psoriasis Area and Severity Index (PASI 50) response maintained their current dosages (15 mg per week maximum) for the duration of the study. However, at week 8, patients who did not achieve a PASI 50 response had their dosage increased to 20 mg per week. By week 12, only patients not achieving a PASI 50 response and who had a < PASI 50 response at week 8 underwent further dosage increase to 25 mg per week for the duration of the study. Patients who achieved ≥ PASI 50 responses at week 12 maintained their current dosages (20 mg per week maximum) for the duration of the study. Oral medication dosages were also adjusted to alanine aminotransferase, aspartate aminotransferase, serum creatinine and blood cell count between week 2 and week 15, if necessary, and could be withheld or reduced at any time, as deemed appropriate by the safety assessors

§ Adalimumab, alefacept, etanercept, infliximab, ustekinumab

|| PUVA

¶ CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

** CyA, corticosteroids, MTX, retinoids

Abbreviations: 8-MOP=8-methoxypsoralen; ALT=alanine aminotransferase;AST=aspartate aminotransferase; BMI=body mass index; BSA=body surface area; CHF=congestive heart failure; CNS=central nervous system; CyA=cyclosporin; d=day(s); dL=deciliter(s); DLQI=Dermatology Life Quality Index; EQ-5D=EuroQOL 5D; h=hour(s); HBV= hepatitis B virus; HCV= hepatitis C virus; HIV=human immunodeficiency virus; HRQoL=health related quality of life; IL=interleukin; IM=intramuscular; IV=intravenous;kg=kilogram(s); L=liter;mg=milligram(s); mm=millimeter(s); mmol=millimol(s); MTX=methotrexate; NA=not applicable; NBUVA=narrowband ultraviolet A; NBUVB=narrowband ultraviolet B;NR=not reported; NS=not specified; OLE=open label extension; PASI=Psoriasis Area and Severity Index; PGA=Physician's Global Assessment; PO=by mouth; PsA=psoriatic arthritis; PUVA=psoralen plus ultraviolet A; QD=daily; RCT=randomized controlled trial; SC=subcutaneous; TB=tuberculosis; TC=total cholesterol; TG=triglycerides; TNF=tumor necrosis factor; UVA=ultraviolet A; VAS=visual analog scale; vs.=versus; w=week(s); y=year(s)

Appendix F. Evidence Tables

Table 5. Final health outcomes (1)

Study, year	Study group	Followup	Total mortality n/N	MACE n/N	Diabetes n/N	Psychological comorbidities* n/N	
Barker, 2011	Infliximab	10w	---	---	---	---	
		16w	---	---	---	---	
		26w†	---	0/649‡	1/649	---	
	MTX	10w	---	---	---	---	---
		16w	---	---	---	---	---
		26w†	---	1/211‡	0/211	---	
	Infliximab transitioned to MTX	26w	---	0/9‡	0/9	---	
	MTX transitioned to infliximab	26w	---	0/63‡	0/63	---	
Inzinger, 2011	Adalimumab	---	---	---	---	---	
	Alefacept	---	---	---	---	---	
	Etanercept	---	---	---	---	---	
	Infliximab	---	---	---	---	---	
	Ustekinumab	---	---	---	---	---	
	PUVA	---	---	---	---	---	
Strober, 2011	MTX transitioned to adalimumab	4w	---	---	---	---	
		16w	0/41	---	---	---	
	NB-UVB transitioned to adalimumab	4w 16w	---	---	---	---	
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	
Caproni, 2009	Etanercept	---	---	---	---	---	
	Acitretin	---	---	---	---	---	
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept§	---	---	---	---	---	
Gisondi, 2008a	Etanercept	---	---	---	---	---	
	Acitretin	---	---	---	---	---	
Gisondi, 2008b	Etanercept	---	---	---	---	---	
	Infliximab	---	---	---	---	---	
	MTX	---	---	---	---	---	

Study, year	Study group	Followup	Total mortality n/N	MACE n/N	Diabetes n/N	Psychological comorbidities* n/N
Saurat, 2008	Adalimumab	12w	---	---	---	---
		16w	---	---	---	
		70d	0/107	---	---	---
	MTX	12w	---	---	---	---
		16w	---	---	---	---
		70d	0/110	---	---	---
	MTX transitioned to adalimumab	---	---	---	---	
Magliocco, 2007	CyA transitioned to alefacept	13w	---	---	---	---
		25w	---	---	---	
		37w	---	---	---	
		48w	---	---	---	
Costanzo, 2005	Nonbiologics transitioned to etanercept¶	---	---	---	---	

Abbreviations: CyA=cyclosporine; d=day(s); MACE=major adverse cardiovascular event; MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B; PUVA=psoralen plus ultraviolet A; w=week(s); ---=not reported

* Includes depression or suicide

† Includes events through week 16 for patients who switched treatments and through week 26 for others who did not

‡ Myocardial infarction

§ CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

|| 70 days after last treatment

¶ CyA, corticosteroids, MTX, retinoids

Table 6. Final health outcomes (2)

Study, year	Study group	Followup	DLQI* mean(SD)	HAQ-DI mean(SD)	EQ-5D† mean(SD)	SF-36 mean(SD)	Other reported outcomes
Barker, 2011	Infliximab	10w	-11.4(NR)	---	0.86(NR)	5.15(NR)§, 7.94(NR)	---
		16w	-11.6(NR)	---	0.86(NR)	5.53(NR)§	---
		26w‡	-11.3(NR)	---	0.86(NR)	---	---
	MTX	10w	-7.9(NR)	---	0.81(NR)	3.00(NR)§, 5.63(NR)	---
		16w	-8.95(NR)	---	0.84(NR)	3.76(NR)§	---
		26w‡	-9.14(NR)	---	0.81(NR)	---	---
	Infliximab transitioned to MTX	---	---	---	---	---	
	MTX transitioned to infliximab	---	---	---	---	---	
Inzinger, 2011	Adalimumab	---	---	---	---	---	---
	Alefacept	---	---	---	---	---	---
	Etanercept	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---
	Ustekinumab	---	---	---	---	---	---
	PUVA	---	---	---	---	---	---
Strober, 2011	MTX transitioned to adalimumab	4w	-4.8(5.89)	---	---	---	---
		16w	-7.0(7.45)	---	---	---	0.7(3.4)** -4.0(28.1)†† -5.5(30.3)‡‡ -13.3(33.1)§§
	NB-UVB transitioned to adalimumab	4w	-5.2(5.45)	---	---	---	---
		16w	-6.5(6.44)	---	---	---	1.3(4.8)** -6.4(19.8)†† -8.0(19.4)‡‡ -12.2(25.6)§§
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	
Caproni, 2009	Etanercept	---	---	---	---	---	
	Acitretin	---	---	---	---	---	
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept	---	---	---	---	---	
Gisondi, 2008a	Etanercept	---	---	---	---	---	
	Acitretin	---	---	---	---	---	

Study, year	Study group	Followup	DLQI* mean(SD)	HAQ-DI mean(SD)	EQ-5D† mean(SD)	SF-36 mean(SD)	Other reported outcomes
Gisondi, 2008b	Etanercept	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---
	MTX	---	---	---	---	---	---
Saurat, 2008	Adalimumab	12w	-9.1(-10.4, -7.8)¶¶	---	IS: 0.2(0.1, 0.2)¶¶ VAS: 20.4(15.3, 25.4)¶¶	---	---
		16w	-9.1(-10.4, -7.8)¶¶	---	IS: 0.2(0.2, 0.3)¶¶ VAS: 21.4(16.6, 26.3)¶¶	---	---
		70d¶	---	---	---	---	---
	MTX	12w	-4.9(-5.9, -3.8)¶¶	---	IS: 0.1(0.1, 0.2)¶¶ VAS: 10.2(5.3, 15.2)¶¶	---	---
		16w	-5.7(-6.8, -4.5)¶¶	---	IS: 0.1(0.1, 0.2)¶¶ VAS: 11.5(6.5, 16.5)¶¶	---	---
		70d¶	---	---	---	---	---
MTX transitioned to adalimumab	---	---	---	---	---	---	
Magliocco, 2007	CyA transitioned to alefacept	0w	3.18(NR)***	---	---	---	---
		13w	1.09(NR)***	---	---	---	---
		25w	4.88(NR)***	---	---	---	---
		37w	3.14(NR)***	---	---	---	---
		48w	3.83(NR)***	---	---	---	---
Costanzo, 2005	Nonbiologics transitioned to etanercept†††	---	---	---	---	---	---

Abbreviations: CyA=cyclosporine; d=day(s); DLQI=Dermatology Life Quality Index; EQ-5D=EuroQoL-5D; HAQ-DI= Health Assessment Questionnaire Disability Index; IS=index score; MACE=major adverse cardiovascular event; MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B; NR=not reported; PUVA=psoralen plus ultraviolet A; SD=standard deviation; SF-36=Short form-36; VAS=visual analogue scale; w=week(s); ---=not reported

* Mean(SD) change from baseline, unless otherwise noted

† Mean(SD) composite score, unless otherwise noted

‡ Includes patients who switched treatments at week 16 as nonresponders

§ Mean(SD) change from baseline in Physical Component Score of SF-36

|| Mean(SD) change from baseline in Mental Component Score of SF-36

¶ 70 days after last treatment

** Mean(SD) change from baseline in percent work time missed due to psoriasis

†† Mean(SD) change from baseline in percent overall work impairment due to psoriasis

‡‡ Mean(SD) change from baseline in percent impairment while working due to psoriasis

§§ Mean(SD) change from baseline in percent activity impairment due to psoriasis

||| CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

¶¶ Mean(95% confidence interval) change from baseline

*** Mean(SD) DLQI score

††† CyA, corticosteroids, MTX, retinoids

Table 7. Intermediate health outcomes (1)

Study, year	Study group	Followup	BSA mean(SD)	PGA* n/N	Patient's Assessment of Global Improvement mean(SD)	Symptom improvement		
						Pruritus†	Pain‡	Other
Barker, 2011	Infliximab	16w	---	496/653	---	---	---	---
		26w§	---	477/653	---	---	---	---
	MTX	16w	---	82/215	---	---	---	---
		26w§	---	60/215	---	---	---	---
	Infliximab transitioned to MTX	18w	---	0/9	---	---	---	---
		22w	---	1/9	---	---	---	---
26w		---	2/9	---	---	---	---	
MTX transitioned to infliximab	18w	---	19/63	---	---	---	---	
	22w	---	45/63	---	---	---	---	
	26w	---	47/63	---	---	---	---	
Inzinger, 2011	Adalimumab	---	---	---	---	---	---	---
	Alefacept	---	---	---	---	---	---	---
	Etanercept	---	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---	---
	Ustekinumab	---	---	---	---	---	---	---
	PUVA	---	---	---	---	---	---	---
Strober, 2011	MTX transitioned to adalimumab	0w	---	1/41	---	---	---	---
		2w	---	0/41	---	---	---	---
		4w	---	13/41	---	---	---	---
		8w	---	22/41	---	---	---	---
		16w	---	25/41	---	---	-2.9(3.9)	-14.7(24.4)
					61% (95%CI 45 to 76)			
	NB-UVB transitioned to adalimumab	0w	---	0/29	---	---	---	---
		2w	---	3/29	---	---	---	---
		4w	---	6/29	---	---	---	---
		8w	---	13/29	---	---	---	---
		16w	---	14/29	---	---	-3.0(2.96)	-21.4(30.0)
					48% (95%CI 29 to 67)			
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	---	---
Caproni, 2009	Etanercept	---	---	---	---	---	---	---
	Acitretin	---	---	---	---	---	---	---
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept¶	---	---	---	---	---	---	---

Study, year	Study group	Followup	BSA mean(SD)	PGA* n/N	Patient's Assessment of Global Improvement mean(SD)	Symptom improvement		
						Pruritus†	Pain‡	Other
Gisondi, 2008a	Etanercept	24w	-80.0%**	---	---	---	---	---
	Acitretin	24w	-45.8%**	---	---	---	---	---
Gisondi, 2008b	Etanercept	---	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---	---
	MTX	---	---	---	---	---	---	---
Saurat, 2008	Adalimumab	4w	---	17/108	---	---	---	---
		8w	---	52/108	---	---	---	---
		12w	---	72/108	---	---	---	---
		16w	---	79/108	-1.6(NR)††	-5.0(NR)	-24.2(NR)	---
	MTX	4w	---	4/110	---	---	---	---
		8w	---	10/110	---	---	---	---
		12w	---	24/110	---	---	---	---
		16w	---	33/110	-1.2(NR)††	-3.5(NR)	-11.1(NR)	---
MTX transitioned to adalimumab	---	---	---	---	---	---	---	
Magliocco, 2007	CyA transitioned to alefacept	13w	---	---	---	---	---	---
		25w	---	4.75(NR)‡‡	---	---	---	---
		37w	---	4.33(NR)‡‡	---	---	---	---
		48w	---	4.33(NR)‡‡	---	---	---	---
Costanzo, 2005	Nonbiologics transitioned to etanercept§§	---	---	---	---	---	---	---

Abbreviations: BSA=body surface area; CI=confidence interval; CyA=cyclosporine; MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B; NR=not reported; PASI=Psoriasis Area and Severity Index; PGA=Physician's Global Assessment; PUVA=psoralen plus ultraviolet A; SD=standard deviation; VAS=visual analog scale; w=week(s); ---=not reported

* Number of patients achieving a PGA score of "clear" or "minimal", unless otherwise noted

† Mean(SD) change from baseline in Psoriasis-related Pruritus Assessment

‡ Mean(SD) change from baseline in VAS for pain involving psoriatic plaques and/or psoriatic arthritis

§ Includes patients who switched treatments at week 16 as nonresponders

|| 95%CI reported as percentage of respective population

¶ CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

** Mean percentage change from baseline

†† Mean(SD) change from baseline

‡‡ Mean(SD) PGA

§§ CyA, corticosteroids, MTX, retinoids

Table 8. Intermediate health outcomes (2)

Study, year	Study group	Followup	PASI50 n/N	PASI75 n/N	PASI90 n/N	PASI100 n/N	PASI mean(SD)	
Barker, 2011	Infliximab	2w	247/653	59/653	11/653	---	---	
		6w	535/653	365/653	150/653	---	---	
		10w	579/653	487/653	291/653	---	---	
		14w	562/653	473/653	310/653	---	---	
		16w	567/653	508/653	356/653	---	---	
		18w*	543/653	488/653	349/653	---	---	
		22w*	530/653	473/653	306/653	---	---	
		26w*	529/653	502/653	333/653	---	-85%†	
	MTX	2w	19/215	1/215	0/215	---	---	
		6w	80/215	31/215	6/215	---	---	
		10w	118/215	58/215	19/215	---	---	
		14w	131/215	85/215	37/215	---	---	
		16w	130/215	90/215	41/215	---	---	
		18w*	120/215	85/215	39/215	---	---	
		22w*	118/215	82/215	39/215	---	---	
		26w*	103/215	66/215	32/215	---	-54%†	
	Infliximab transitioned to MTX	18w	---	0/9	0/9	---	---	
		22w	---	1/9	0/9	---	---	
		26w	---	1/9	0/9	---	---	
	MTX transitioned to infliximab	18w	---	15/63	5/63	---	---	
		22w	---	38/63	17/63	---	---	
		26w	---	46/63	30/63	---	---	
	Inzinger, 2011‡	Adalimumab	12w	13/18	10/18	4/18	1/18	---
		Alefacept	12w	20/32	8/32	1/32	1/32	---
		Etanercept	12w	32/38	15/38	11/38	2/38	---
		Infliximab	12w	7/7	7/7	5/7	2/7	---
Ustekinumab		12w	16/18	12/18	7/18	1/18	---	
PUVA		10.3w§	65/71	63/71	50/71	15/71	---	
Strober, 2011	MTX transitioned to adalimumab	0w	---	---	---	---	10.8(NR)	
		2w	---	---	---	---	6.9(NR)	
		4w	---	---	---	---	5.4(NR)	
		8w	---	---	---	---	3.4(NR)	
		16w	---	---	---	---	2.3(NR)	
	NB-UVB transitioned to adalimumab	0w	---	---	---	---	12.4(NR)	
		2w	---	---	---	---	9.1(NR)	
		4w	---	---	---	---	6.7(NR)	
		8w	---	---	---	---	4.1(NR)	
		16w	---	---	---	---	3.6(NR)	

Study, year	Study group	Followup	PASI50 n/N	PASI75 n/N	PASI90 n/N	PASI100 n/N	PASI mean(SD)
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	---
Caproni, 2009	Etanercept	12w	26/30	17/30	---	---	4.61(2.75)
	Acitretin	12w	20/30	8/30	---	---	9.62(4.64)
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept	12w	79/98	43/98	---	---	4.9(4.0)
		24w	88/98	74/98	---	---	2.8(3.4)
Gisondi, 2008a	Etanercept	6w	6/22	2/22	---	---	---
		12w	9/22	5/22	---	---	---
		18w	11/22	8/22	---	---	---
		24w	15/22	10/22	---	---	---
	Acitretin	6w	2/20	1/20	---	---	---
		12w	4/20	2/20	---	---	---
		18w	7/20	2/20	---	---	---
		24w	10/20	6/20	---	---	---
Gisondi, 2008b	Etanercept	24w	---	---	---	---	4.8(4.7) -74.5%†
	Infliximab	24w	---	---	---	---	2.1(3.2) -88.8%†
	MTX	24w	---	---	---	---	4.3(6.0) -47.1%†
Saurat, 2008	Adalimumab	2w	---	5/108	---	---	---
		4w	73/108	25/108	7/108	1/108	---
		8w	88/108	67/108	29/108	9/108	---
		12w	98/108	83/108	52/108	12/108	---
		16w	95/108	86/108	56/108	18/108	-16.7(8.8)¶
	MTX	2w	---	0/110	---	---	---
		4w	17/110	3/110	1/110	1/110	---
		8w	42/110	10/110	3/110	0/110	---
		12w	60/110	27/110	10/110	1/110	---
		16w	68/110	39/110	15/110	8/110	-10.9(8.3)¶
	MTX transitioned to adalimumab	0w	---	26/95	13/95	5/95	---
		24w	---	70/95	50/95	30/95	---
Magliocco, 2007	CyA transitioned to alefacept	---	---	---	---	---	
Costanzo, 2005	Nonbiologics transitioned to etanercept**	12w	28/44	19/44	4/44	---	7.5(NR) -52%†
		24w	12/15	10/15	6/15	---	4.3(NR) -72%†

Abbreviations: CyA=cyclosporine; MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B; NR=not reported; PASI=Psoriasis Area and Severity Index; PUVA=psoralen plus ultraviolet A; w=week(s); ---=not reported

* Includes patients who switched treatments at week 16 as nonresponders

† Mean percentage change from baseline

‡ Results reported out of treatment courses, not patients. Patients could have more than one treatment course

§ End of phototherapy treatment, median 10.3w

|| Nonbiologics included CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

¶ Mean(SD) change from baseline

** Nonbiologics included CyA, corticosteroids, MTX, retinoids

Table 9. Adverse outcomes (1)

Study, year	Study group	Followup	Hepatotoxicity n/N		Nephrotoxicity n/N		Hematologic toxicity n/N			
			AST	ALT	SCr	GFR	TCP	Anemia	Neutropenia	
Barker, 2011	Infliximab	26w*	2/649†	---	---	---	---	1/649	---	---
	MTX	26w*	1/211†	---	---	---	---	0/211	---	---
	Infliximab transitioned to MTX	26w	0/9†	---	---	---	---	0/9	---	---
	MTX transitioned to infliximab	26w	0/63†	---	---	---	---	0/63	---	---
Inzinger, 2011	Adalimumab	---	---	---	---	---	---	---	---	---
	Alefacept	---	---	---	---	---	---	---	---	---
	Etanercept	---	---	---	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---	---	---	---
	Ustekinumab	---	---	---	---	---	---	---	---	---
	PUVA	---	---	---	---	---	---	---	---	---
Strober, 2011	MTX transitioned to adalimumab	---	---	---	---	---	---	---	---	---
	NB-UVB transitioned to adalimumab	---	---	---	---	---	---	---	---	---
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	---	---	---	---
Caproni, 2009	Etanercept	---	---	---	---	---	---	---	---	---
	Acitretin	---	---	---	---	---	---	---	---	---
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept‡	---	---	---	---	---	---	---	---	---

Study, year	Study group	Followup	Hepatotoxicity n/N		Nephrotoxicity n/N		Hematologic toxicity n/N		
			AST	ALT	SCr	GFR	TCP	Anemia	Neutropenia
Gisondi, 2008a	Etanercept	---	---	---	---	---	---	---	---
	Acitretin	---	---	---	---	---	---	---	---
Gisondi, 2008b	Etanercept	---	---	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---	---	---
	MTX	---	---	---	---	---	---	---	---
Saurat, 2008	Adalimumab	70d§	0/107	0/107	---	---	---	---	---
	MTX	70d§	2/110	4/110	---	---	---	---	---
	MTX transitioned to adalimumab	---	---	---	---	---	---	---	---
Magliocco, 2007	CyA transitioned to alefacept	---	---	---	---	---	---	---	---
Costanzo, 2005	Nonbiologics	2w	---	---	---	---	---	---	---
	transitioned to	8w	---	---	---	---	1/44	---	---
	etanercept¶	12w	---	---	---	---	---	---	---

Abbreviations: ALT=alanine aminotransferase; AST=aspartate aminotransferase; CyA=cyclosporine; d=day(s); GFR=glomerular filtration rate; MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B; PUVA=psoralen plus ultraviolet A; SCr=serum creatinine; TCP=thrombocytopenia; w=week(s); ---=not reported

* Includes events through week 16 for patients who switched treatments and through week 26 for others who did not

† Hepatic enzyme increases

‡ CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

§ 70 days after last treatment

|| Level greater than 2.5 times upper limit of normal

¶ CyA, corticosteroids, MTX, retinoids

Table 10. Adverse outcomes (2)

Study, year	Study group	Followup	Hypertension n/N	Metabolic alterations n/N				
				Glucose	Lipids	Weight	BMI	Thyroid function
Barker, 2011	Infliximab	26w*	0/649	---	---	---	---	---
	MTX	26w*	0/211	---	---	---	---	---
	Infliximab transitioned to MTX	26w	0/9	---	---	---	---	---
	MTX transitioned to infliximab	26w	1/63	---	---	---	---	---

Study, year	Study group	Followup	Hypertension n/N	Metabolic alterations n/N				
				Glucose	Lipids	Weight	BMI	Thyroid function
Inzinger, 2011	Adalimumab	---	---	---	---	---	---	---
	Alefacept	---	---	---	---	---	---	---
	Etanercept	---	---	---	---	---	---	---
	Infliximab	---	---	---	---	---	---	---
	Ustekinumab	---	---	---	---	---	---	---
	PUVA	---	---	---	---	---	---	---
Strober, 2011	MTX transitioned to adalimumab	---	---	---	---	---	---	---
	NB-UVB transitioned to adalimumab	---	---	---	---	---	---	---
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	---	---
Caproni, 2009	Etanercept	---	---	---	---	---	---	---
	Acitretin	---	---	---	---	---	---	---
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept†	---	---	---	---	---	---	---
Gisondi, 2008a	Etanercept	---	---	---	---	---	---	---
	Acitretin	---	---	---	---	---	---	---
Gisondi, 2008b	Etanercept	24w	---	---	235(17.3)‡	1.5(2.7)§	0.5(0.5)	---
	Infliximab	24w	---	---	237(16.9)‡	2.5(3.3)§	0.8(1.0)	---
	MTX	24w	---	---	236(18.1)‡	-0.6(1.4)§	-0.2(0.5)	---
Saurat, 2008	Adalimumab	---	---	---	---	---	---	---
	MTX	---	---	---	---	---	---	---
	MTX transitioned to adalimumab	---	---	---	---	---	---	---
Magliocco, 2007	CyA transitioned to alefacept	---	---	---	---	---	---	---
Costanzo, 2005	Nonbiologics transitioned to etanercept¶	---	---	---	---	---	---	---

Abbreviations: BMI=body mass index; CyA=cyclosporine; d=day(s); MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B;

PUVA=psoralen plus ultraviolet A; w=week(s); ---=not reported

* Includes events through week 16 for patients who switched treatments and through week 26 for others who did not

† CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

‡ Mean(SD) total cholesterol level

§ Mean(SD) body weight (kg) change from baseline

|| Mean(SD) BMI change from baseline

¶ CyA, corticosteroids, MTX, retinoids

Table 11. Adverse outcomes (3)

Study, year	Study group	Followup	Injection site reaction n/N	Malignancy n/N	Infections n/N	Study withdrawal n/N	
Barker, 2011	Infliximab	26w*	17/649†	1/649‡	10/649§	112/653	
	MTX	26w*	0/211†	0/211‡	4/211§	88/215	
	Infliximab transitioned to MTX	26w	0/9†	0/9	0/9	---	
	MTX transitioned to infliximab	26w	5/63†	0/63	1/63	---	
Inzinger, 2011	Adalimumab	---	---	---	---	---	
	Alefacept	---	---	---	---	---	
	Etanercept	---	---	---	---	---	
	Infliximab	---	---	---	---	---	
	Ustekinumab	---	---	---	---	---	
	PUVA	---	---	---	---	---	
Strober, 2011	MTX transitioned to adalimumab	70d¶	2/41	0/41	13/41** 0/41††	2/41	
	NB-UVB transitioned to adalimumab	70d¶	0/29	0/29	7/29** 1/29††	5/29	
Garavaglia, 2010	CyA transitioned to etanercept	---	---	---	---	---	
Caproni, 2009	Etanercept	12w	---	---	---	0/30	
	Acitretin	12w	---	---	---	0/30	
Mazzotta, 2009	Nonbiologics or phototherapy transitioned to etanercept††	---	---	---	---	---	
Gisondi, 2008a	Etanercept	6w	---	---	---	0/22	
		12w	---	---	---	---	
		24w	---	---	---	---	
	Acitretin	6w	---	---	---	---	4/20
		12w	---	---	---	---	---
		24w	---	---	---	---	---
Gisondi, 2008b	Etanercept	---	---	---	---	---	
	Infliximab	---	---	---	---	---	
	MTX	---	---	---	---	---	

Study, year	Study group	Followup	Injection site reaction n/N	Malignancy n/N	Infections n/N	Study withdrawal n/N
Saurat, 2008	Adalimumab	70d¶	---	---	51/107** 0/107††	4/108
	MTX	70d¶	---	---	46/110** 0/110††	6/110
	MTX transitioned to adalimumab	---	---	---	---	---
Magliocco, 2007	CyA transitioned to alefacept	---	---	0/11	0/11	5/11
Costanzo, 2005	Nonbiologics transitioned to etanercept§§	2w 8w 12w	2/44 --- ---	--- --- ---	--- --- 0/44§	4/44 --- ---

Abbreviations: CyA=cyclosporine; d=day(s); MTX=methotrexate; n/N=number of patients per total population; NB-UVB=narrowband ultraviolet B; PUVA=psoralen plus ultraviolet A; w=week(s); ---=not reported

* Includes events through week 16 for patients who switched treatments and through week 26 for others who did not

† Infusion related reaction

‡ Basal cell carcinoma

§ Includes tuberculosis, opportunistic infections and serious viral infections

|| Includes bacterial arthritis and staphylococcal infection

¶ 70 days after last treatment

** Any infection

†† Any serious infection

‡‡ CyA, corticosteroids, fumaric acid esters, MTX, retinoids, PUVA

§§ CyA, corticosteroids, MTX, retinoids

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Appendix G. Strength of Evidence for Outcomes

Table 12. Strength of evidence for final health outcomes comparing adalimumab with methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (1)	Low risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (1)	Low risk bias	NA	Direct	Precise	Low
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 13. Strength of evidence for intermediate health outcomes comparing adalimumab with methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (1)	Low risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
PGA	RCT (1)	Low risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (1)	Low risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
Individual symptoms-pain	RCT (1)	Low risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
Individual symptoms-puritus	RCT (1)	Low risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 14. Strength of evidence for final health outcomes comparing etanercept versus acitretin

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 15. Strength of evidence for intermediate health outcomes comparing etanercept versus acitretin

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (1)	Low risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (2)	Low risk of bias	Consistent	Direct	NA	Moderate
	Observational (0)	---	---	---	---	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 16. Strength of evidence for final health outcomes comparing etanercept versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 17. Strength of evidence for intermediate health outcomes comparing etanercept versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 18. Strength of evidence for final health outcomes comparing infliximab versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (1)	Medium risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
MACE	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 19. Strength of evidence for intermediate health outcomes comparing infliximab versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (1)	Medium risk of bias	NA	Direct	NA	Low
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (1)	Medium risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 20. Strength of evidence for final health outcomes comparing adalimumab with psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 21. Strength of evidence for intermediate health outcomes comparing adalimumab with psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 22. Strength of evidence for final health outcomes comparing alefacept with psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 23. Strength of evidence for intermediate health outcomes comparing alefacept with psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 24. Strength of evidence for final health outcomes comparing etanercept with psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 25. Strength of evidence for intermediate health outcomes comparing etanercept with psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 26. Strength of evidence for final health outcomes comparing infliximab versus psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 27. Strength of evidence for intermediate health outcomes comparing infliximab versus psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 28. Strength of evidence for final health outcomes comparing ustekinumab versus psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Mortality	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
HRQoL	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
MACE	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Diabetes	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Psychological Comorbidities	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

HRQoL= health-related quality of life; MACE=major cardiovascular events; NA=not applicable; RCT=randomized controlled trials

Table 29. Strength of evidence for intermediate health outcomes comparing ustekinumab versus psoralen plus ultraviolet A

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precisions	Strength of Evidence
Plaque BSA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
PASI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
PGA	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Patient assessment of disease	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Individual symptoms	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 30. Strength of evidence for harms comparing adalimumab versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (1)	Low risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hematologic toxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Alterations in metabolic parameters	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Injection site reaction	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Malignancy	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Infection	RCT (1)	Low risk of bias	NA	Direct	NA	Low
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (1)	Low risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	

NA=not applicable; RCT=randomized controlled trial

Table 31. Strength of evidence for harms comparing alefacept versus cyclosporine

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hematologic toxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Alterations in metabolic parameters	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Injection site reaction	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Malignancy	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Infection	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 32. Strength of evidence for harms comparing etanercept versus acitretin

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (1)	Low risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hematologic toxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Alterations in metabolic parameters	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Injection site reaction	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Malignancy	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Infection	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (2)	Medium risk of bias	Inconsistent	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 33. Strength of evidence for harms comparing etanercept versus cyclosporine

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hematologic toxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (0)	---	---	---	---	Insufficient

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
	Observational (0)	---	---	---	---	
Alterations in metabolic parameters	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Injection site reaction	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Malignancy	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Infection	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 34. Strength of evidence for harms comparing etanercept versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hematologic toxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Total cholesterol	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
Weight and BMI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
Injection site reaction	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Malignancy	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Infection	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 35. Strength of evidence for harms comparing infliximab versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Thrombocytopenia	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Total cholesterol	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
Weight and BMI	RCT (0)	---	---	---	---	Insufficient
	Observational (1)	Medium risk of bias	NA	Direct	NA	
Injection site reaction	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Malignancy	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Infection	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (1)	Medium risk of bias	NA	Direct	NA	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Table 36. Strength of evidence for harms comparing infliximab versus methotrexate

Outcome	Study design and number	Risk of bias	Consistency	Directness	Precision	Strength of Evidence
Hepatotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Nephrotoxicity	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Thrombocytopenia	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Hypertension	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Total cholesterol	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Weight and BMI	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Injection site reaction	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Malignancy	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Infection	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	
Study withdrawal	RCT (0)	---	---	---	---	Insufficient
	Observational (0)	---	---	---	---	

BSA=body surface area; NA=not applicable; PASI=Psoriasis Area Severity Index; PGA=Physician's Global Assessment; RCT=randomized controlled trial

Appendix H. Applicability of Individual Studies

Table 37. Evaluation of applicability for individual randomized controlled trials

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Barker, 2011	Study Designation: Effectiveness study Composite Score: 6 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Assessed final health outcomes 3. Adequate study duration with clinically relevant treatments 4. Assessed adverse outcomes 5. Adequate sample size 6. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Duration of followup for final health outcomes (MACE, diabetes – 26 weeks) • Duration of followup for adverse outcomes (malignancy, infections – 26 weeks) • Conducted in Europe
Caproni, 2009	Study Designation: Efficacy study Composite Score: 3 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Did not assess final health outcomes • Duration of followup for intermediate health outcomes (PASI – 12 weeks) • Inadequate sample size • Conducted in Italy
Gisondi, 2008a	Study Designation: Efficacy study Composite Score: 4 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Adequate study duration with clinically relevant treatments 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Did not assess final health outcomes • Inadequate sample size • Conducted in Italy
Saurat, 2008	Study Designation: Effectiveness study Composite Score: 6 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Assessed final health outcomes 3. Adequate study duration with clinically relevant treatments 4. Assessed adverse outcomes 5. Adequate sample size 6. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Duration of followup for final health outcomes (mortality – 70 days after last treatments) • Duration of followup for adverse events (infections – 70 days after last followup) • Conducted in Europe and Canada

Table 38. Evaluation of applicability for individual observational studies

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Inzinger, 2011	Study Designation: Efficacy study Composite Score: 3 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis 	Intervention, Outcomes, Setting	<ul style="list-style-type: none"> • Did not report final health outcomes • Duration of followup for intermediate outcomes (PASI – 12 weeks) • Did not report adverse events • Inadequate sample size • Conducted in Austria
Strober, 2011	Study Designation: Effectiveness study Composite Score: 5 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Assessed final health outcomes 3. Adequate study duration with clinically relevant treatments 4. Assessed adverse outcomes 5. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Duration of followup for final health outcomes (mortality – 16 weeks) • Duration of followup for adverse events (malignancy, infections – 16 weeks) • Inadequate sample size • Multicenter study with the US included
Garavaglia, 2010	Study Designation: Efficacy study Composite Score: 2 of 7	<ol style="list-style-type: none"> 1. Assessed adverse outcomes 2. Used intention-to-treat analysis 	Population, Intervention, Outcomes, Setting	<ul style="list-style-type: none"> • High male to female ratio (M: 75%, F: 25%) • More stringent eligibility criteria • Did not assess final health outcomes • Duration of followup for intermediate health outcomes (PASI – 12 weeks) • Inadequate sample size • Conducted in Italy
Mazzotta, 2009	Study Designation: Efficacy study Composite Score: 3 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Adequate study duration with clinically relevant treatments 3. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Did not assess final health outcomes • Did not assess adverse events • Inadequate sample size • Conducted in Italy
Gisondi, 2008b	Study Designation: Efficacy study Composite Score: 4 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Adequate study duration with clinically relevant treatments 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 	Population, Intervention, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Did not assess final health outcomes • Inadequate sample size • Conducted in Italy

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Magliocco, 2007	Study Designation: Efficacy study Composite Score: 4 of 7	<ol style="list-style-type: none"> 1. Assessed final health outcomes 2. Adequate study duration with clinically relevant treatments 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 	Population, Outcomes	<ul style="list-style-type: none"> • Male to female ratio not reported • More stringent eligibility criteria • Duration of followup for adverse events (malignancy, infection – NR) • Inadequate sample size
Costanzo, 2005	Study Designation: Efficacy Study Composite Score: 4 of 7	<ol style="list-style-type: none"> 1. Enrolled primary care population 2. Adequate study duration with clinically relevant treatments 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 	Population, Outcomes, Setting	<ul style="list-style-type: none"> • More stringent eligibility criteria • Did not assess final health outcomes • Duration of followup for adverse events (infection – 12 weeks) • Inadequate sample size • Conducted in Italy

Abbreviations: F=female(s); M=male(s); MACE=major adverse cardiovascular event; NR=not reported; PASI=Psoriasis Area and Severity Index

Appendix I. Glossary

Body mass index (BMI): A measure of body fat based on height and weight that applies to adult men and women. There are four categories including underweight (≤ 18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (≥ 30).

Body surface area (BSA): Estimation of BSA affected by psoriasis may be done by using hand area representing approximately 1% of total body surface.

Confidence Intervals (CIs): The range within which the ‘true’ value (e.g. size of effect of an intervention) would be expected to lie if sampling could be repeated a large number of times (e.g. 95% or 99%).

Dermatology Life Quality Index (DLQI): A 10-item dermatology-specific validated questionnaire which assesses the health related quality of life of patients suffering from a particular skin condition. All questions refer to “over the past week”. Scores range from 0 (no effect at all on patient’s life) to 30 (extremely large effect on patient’s life). A 5-point reduction is considered clinically relevant.

EuroQoL-5D (EQ-5D): A standardized instrument for use as a measure of health outcomes; it is utilized in a wide variety of disease states. EQ-5D utility index is scaled between 0 (dead) and 1 (optimal health).

Glomerular filtration rate (GFR): A measure of the overall index of kidney function where the normal GFR varies according to age, sex, and body size, and declines with age.

Health Assessment Questionnaire (HAQ): An assessment of patient-oriented outcomes based on five dimensions including disability, pain, medication effects, costs of care, and mortality. There are two HAQ versions including the Full HAQ, which assesses all of the five dimensions, and the Short HAQ, which contains only the HAQ disability index (HAQ-DI) and the HAQ’s patient global and pain visual analog scales (VAS).

Health Assessment Questionnaire Disability Index (HAQ-DI): A 20 question, eight category assessment of a patient’s level of functional ability and includes questions of fine movements of the upper extremity, locomotor activities of the lower extremity, and activities that involve both upper and lower extremities. Patient responses are based on a scale from zero, representing no disability, to three, corresponding to complete disability.

Health-Related Quality-of-Life (HRQoL): A person or cohort’s perceived physical and mental health over time. Often assessed in chronic plaque psoriasis evaluations using the Dermatology Life Quality Index (DLQI), 36-item Medical Outcomes Study Short-Form General Health Survey (SF-36) or other disease-specific or general measures.

Intention to treat (ITT): One in which all of the participants in a trial are analysed according to the intervention to which they were allocated, whether they received it or not.

Major adverse cardiac events (MACE): Psoriasis, an inflammatory skin disease, if severe, has been observed to be a risk factor for cardiovascular disease; however, the degree of the association with MACE, such as myocardial infarction, stroke and cardiovascular death, has not been defined.

Meta-Analysis: The process of extracting and pooling data from several studies investigating a similar topic to synthesize a final outcome.

Neutralizing antibodies: A phenomenon observed with prolonged therapy of TNF-alpha inhibitors, including infliximab (Remicade), adalimumab (Humira), and etanercept (Enbrel),

which may lead to the development of autoantibodies that counteract the TNF-alpha antagonist activity of the drugs and reduces efficacy.

Patient's Assessment of Global Improvement: A measure of patient's impression of how well his/her disease is controlled. The score ranges from 0 (complete disease control) to 3 (uncontrolled disease).

Percent activity impairment due to psoriasis: Percent impairment in regular activities was evaluated using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP), a 6-item questionnaire that measures effect of psoriasis on daily activity impairment, number of hours worked and the number of hours missed from work. Scores range from 0% to 100%. A decrease in percent impairment indicates improvement.

Percent impairment while working due to psoriasis: Percent impairment while working was evaluated using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP), a 6-item questionnaire that measures effect of psoriasis on daily activity impairment, number of hours worked and the number of hours missed from work. Scores range from 0% to 100%. A decrease in percent impairment indicates improvement.

Percent overall work impairment due to psoriasis: Percent overall work impairment was evaluated using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP), a 6-item questionnaire that measures effect of psoriasis on daily activity impairment, number of hours worked and the number of hours missed from work. Scores range from 0% to 100%. A decrease in percent overall work impairment indicates improvement.

Percent work time missed due to psoriasis: Percent work time missed due to psoriasis was evaluated using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP), a 6-item questionnaire that measures effect of psoriasis on daily activity impairment, number of hours worked and the number of hours missed from work. Scores range from 0% to 100%. A decrease in percent work time missed indicates improvement.

Physician's Global Assessment (PGA): A 6-point scale used to measure the severity of a patient's disease relative to baseline condition by a dermatologist. Overall lesions are graded for induration, erythema, and scaling. The score ranges from 0=clear (no plaque elevation; no scaling; erythema=hyperpigmentation, pigmented macules, diffuse faint pink or red coloration) to 5=very severe (plaque elevation=very marked; scaling=very coarse; erythema=very severe). A 7-point scale also available with 7 being clear and 6 almost clear, 5 mild, 4 mild to moderate, 3 moderate, 2 moderately severe and 1 being severe psoriasis.

Plaque psoriasis: The most common form of psoriasis, also known as psoriasis vulgaris, recognized by red, raised lesions covered by silvery scales. About 80% of patients with psoriasis have this type.

Psoriasis Area and Severity Index (PASI): A clinical assessment of the severity and extent of disease based on body surface area involvement, erythema, induration, and scaling. The PASI score is commonly used to assess efficacy of psoriasis treatments. The score ranges from 0 (no disease) to 72 (maximal disease). An improvement of 50%, 75%, 90%, 100% from baseline corresponds to PASI 50, PASI 75, PASI 90, and PASI 100, respectively. An improvement of 75% from baseline (PASI 75) is commonly used as a dichotomous cut-off for efficacy in most trials.

Psoriatic Arthritis: Rheumatoid factor-negative inflammatory arthritis associated with psoriasis. This disease is characterised by stiffness, pain, and swelling in the joints, especially of the hands and feet. It affects about 23% of people with psoriasis. Early diagnosis and treatment can help inhibit the progression of joint deterioration.

Psoriasis-related Pruritus Assessment: A scale for evaluating pruritus-related to psoriasis over the previous week; values range from 0 (no itching) to 10 (severe itching). A decrease in score indicates an improvement in pruritus.

Relative Risks (RRs): The ratio of an event occurring in an exposed group to an event occurring in a non-exposed group in a given population. A ratio of one indicates no difference in the risk between the two groups.

Sensitivity Analyses: A ‘what if’ analysis that helps determine the robustness of a study. Helps determine the degree of importance of each variable for a given outcome.

Standard Deviations (SDs): A measure of the variability of a data set.

Thrombocytopenia: A condition where there is an abnormally low amount of platelets (<50,000 platelets/microliter), components of the blood that assist in clotting, which may lead to abnormal bleeding. Normal human platelet count ranges from 150,000 to 450,000 platelets per microliter of blood.

Tumor necrosis factor (TNF): One of the cytokines, or messengers, known to be fundamental to the disease process that underlies psoriasis. It often plays a key role in the onset and the continuation of skin inflammation.

TNF-alpha inhibitors: Agents that bind to and neutralize the effects of TNF-alpha, a pro-inflammatory cytokine, by preventing its binding to receptors. FDA-approved agents for use in plaque psoriasis include infliximab (Remicade), etanercept (Enbrel), and adalimumab (Humira).

Variance: A measure of the variation shown by a set of observations, defined by the sum of the squares of deviations from the mean, divided by the number of degrees of freedom in the set of observations.

Visual analogue scale (VAS): Direct rating where raters are asked to place a mark at a point between two anchor states appearing at either end of the line. It is used as a method of valuing health states.

Visual analogue scale (VAS) for plaque psoriasis and psoriatic arthritis pain: A scale for evaluating pain due to plaque psoriasis and psoriatic arthritis during the previous week; values range from 0 (no pain) to 100 (pain as bad as it could be). A decrease in score indicates an improvement in pain.

Appendix J. Abbreviations

ALT = aspartate aminotransferase
AST= alanine aminotransferase
BMI=body mass index
BSA = body surface area
CI = confidence interval
DLQI = dermatology life quality index
EQ-5D = EuroQolTM-5 Dimension
Kg = kilogram
Kg/m²=kilogram per meter squared
HRQoL = health-related quality of life
MACE = major adverse cardiovascular events
NB-UVB = narrowband-ultraviolet B
NR = not reported
RCT = randomized controlled trial
PASI = Psoriasis Area and Severity Index
PGA = Physician's Global Assessment
PsA = psoriatic arthritis
PUVA = psoralen plus ultraviolet A
SCr = serum creatinine
SF-36 = Short Form-36 Health Survey
TCP = thrombocytopenia
TNF = tumor necrosis factor
ULN = upper limit of normal
VAS = visual analogue scale
8-MOP = 8-methoxypsoralen