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Appendix S1

References included in the Forest plot

1. Akçali C, Guven EH, Kirtak N, Inaloz HS, Ozgoztasi O, Guvenc U. Serum concentrations of interleukin-2 and tumour necrosis factor- α under cyclosporine versus acitretin treatment in plaque-type psoriasis. *J Int Med Res* 2014; 42: 1118-22.
2. Bagatin E, Parada MOB, Miot HA, Hassun KM, Michalany N, Talarico S. A randomized and controlled trial about the use of oral isotretinoin for photoaging. *Int J Dermatol* 2010; 49: 207-14.
3. Bavinck JN, Tieben LM, Van der Woude FJ, Tegzess AM, Hermans J, ter Schegget J, et al. Prevention of skin cancer and reduction of keratotic skin lesions during acitretin therapy in renal transplant recipients: a double-blind, placebo-controlled study. *J Clin Oncol*. 1995; 13: 1933-8.
4. Butler DF, Parekh PK, Lenis A. Imiquimod 5% cream as adjunctive therapy for primary, solitary, nodular nasal basal cell carcinomas before Mohs micrographic surgery: a randomized, double blind, vehicle-controlled study. *Dermatol Surg* 2009; 35: 24-9.
5. Caproni M, Antiga E, Melani L, Volpi W, Del Bianco E, Fabbri P. Serum levels of IL-17 and IL-22 are reduced by etanercept, but not by acitretin, in patients with psoriasis: a randomized-controlled trial. *J Clin Immunol* 2009; 29: 210-4.
6. Dytoc M, Wat H, Cheung-Lee M, Sawyer D, Ackerman T, Fiorillo L. Evaluation of the efficacy and safety of topical imiquimod 5% for plaque-type morphea: a multicenter, prospective, vehicle-controlled trial. *J Cutan Med Surg* 2015; 19: 132-9.
7. Ertl GA, Levine N, Kligman AM. A comparison of the efficacy of topical tretinoin and low-dose oral isotretinoin in rosacea. *Arch Dermatol* 1994; 130: 319-24.
8. Gaeta GM, Gombos F, Femiano F, Battista C, Minghetti P, Montanari L, et al. Acitretin and treatment of the oral leucoplakias. A model to have an active molecules release. *J Eur Acad Dermatol Venereol* 2000; 14: 473-8.
9. Gahalaut P, Soodan PS, Mishra N, Rastogi MK, Soodan HS, Chauhan S. Clinical efficacy of psoralen + sunlight vs. combination of isotretinoin and psoralen + sunlight for the treatment of chronic plaque-type psoriasis vulgaris: a randomized hospital-based study. *Photodermat Photoimmunol Photomed* 2014; 30: 294-301.
10. Gebauer K, Shumack S, Cowen PSJ. Effect of dosing frequency on the safety and efficacy of imiquimod 5% cream for treatment of actinic keratosis on the forearms and hands: a phase II, randomized placebo-controlled trial. *Br J Dermatol* 2009; 161: 897-903.

11. Georgala S, Katoulis AC, Georgala C, Bozi E, Mortakis A. Oral isotretinoin in the treatment of recalcitrant condylomata acuminata of the cervix: a randomised placebo controlled trial. *Sex Transm Infect* 2004; 80: 216-8.
12. Gisondi P, Del Giglio M, Cotena C, Girolomoni G. Combining etanercept and acitretin in the therapy of chronic plaque psoriasis: a 24-week, randomized, controlled, investigator-blinded pilot trial. *Br J Dermatol* 2008; 158: 1345-9.
13. Goldenberg G, Linkner RV, Singer G, Frankel A. An investigator-initiated study to assess the safety and efficacy of Imiquimod 3.75% cream when used after cryotherapy in the treatment of hypertrophic actinic keratoses on dorsal hands and forearms. *J Clin Aesthet Dermatol* 2013; 6: 36-43.
14. Gollnick H, Blume-Peytavi U, Szabó EL, Meyer KG, Hauptmann P, Popp G, et al. Systemic isotretinoin in the treatment of rosacea - doxycycline- and placebo-controlled, randomized clinical study. *J Dtsch Dermatol Ges* 2010; 8: 505-15.
15. Grimm C, Polterauer S, Natter C, Rahhal J, Hebler L, Tempfer CB, et al. Treatment of cervical intraepithelial neoplasia with topical imiquimod: a randomized controlled trial. *Obstet Gynecol* 2012; 120: 152-9.
16. Gupta, S, Dar, L, Kumar, P, Sharma, V, Verma, K, and Dwivedi, SN. Efficacy and safety of intralesional (IL) injection of mycobacterium w Vaccine Vs. Imiquimod Cream in the treatment of anogenital warts: a double blind randomised trial. *Sexually transmitted infections* 2013; 89.
17. Hung IFN, Zhang AJ, To KKW, Chan JFW, Li C, Zhu HS, et al. Immunogenicity of intradermal trivalent influenza vaccine with topical imiquimod: a double blind randomized controlled trial. *Clin Infect Dis* 2014; 59: 1246-55.
18. Hung IFN, Zhang AJ, To KKW, Chan JFW, Li P, Wong TL, et al. Topical imiquimod before intradermal trivalent influenza vaccine for protection against heterologous non-vaccine and antigenically drifted viruses: a single-centre, double-blind, randomised, controlled phase 2b/3 trial. *Lancet Infect Dis* 2016; 16: 209-18.
19. Ioannides D, Lazaridou E, Apalla Z, Sotiriou E, Gregoriou S, Rigopoulos D. Acitretin for severe lichen sclerosus of male genitalia: a randomized, placebo controlled study. *J Urol* 2010; 183: 1395-9.
20. Kadakia KC, Barton DL, Loprinzi CL, Sloan JA, Otley CC, Diekmann BB, et al. Randomized controlled trial of acitretin versus placebo in patients at high-risk for basal cell or squamous cell carcinoma of the skin (North Central Cancer Treatment Group Study 969251). *Cancer* 2012; 118: 2128-37.
21. Kumar P, Dar L, Saldiwal S, Varma S, Datt Upadhyay A, Talwar D, et al. Intralesional injection of Mycobacterium w vaccine vs imiquimod, 5%, cream in patients with anogenital warts: a randomized clinical trial. *JAMA Dermatol* 2014; 150: 1072-8.

22. Lecluse LLA, Spuls PI. Photodynamic therapy versus topical imiquimod versus topical fluorouracil for treatment of superficial basal-cell carcinoma: a single blind, non-inferiority, randomised controlled trial: a critical appraisal *Br J Dermatol* 2015; 172: 8-10.
23. Morales Toquero A, Ocampo Candiani J, Gomez Flores M, Gonzalez Gonzalez SE, Eguia Rodriguez R, Mendez Olvera NP. Clinical and histological evaluation of 5% imiquimod cream vs 5% 5-fluorouracil ointment in patients with actinic keratosis on the face. *Dermatologia: revista mexicana* 2010; 54: 326-331.
24. Mortazavi H, Khezri S, Hosseini H, Khezri F, Vasigh M. A single blind randomized clinical study: the efficacy of isotretinoin plus narrow band ultraviolet B in the treatment of psoriasis vulgaris. *Photodermatol Photoimmunol Photomed* 2011; 27: 159-61.
25. Olguin-García MG, Jurado-Santa Cruz F, Peralta-Pedrero ML, Morales-Sánchez MA. A double-blind, randomized, placebo-controlled trial of oral isotretinoin in the treatment of recalcitrant facial flat warts. *J Dermatolog Treat* 2015; 26: 78-82.
26. Olsen EA, Kelly FF, Vollmer RT, Buddin DA, Weck PK. Comparative study of systemic interferon alfa-1n and isotretinoin in the treatment of resistant condylomata acuminata. *J Am Acad Dermatol* 1989; 20: 1023-30.
27. Oprica C, Emtestam L, Hagströmer L, Nord CE. Clinical and microbiological comparisons of isotretinoin vs. tetracycline in acne vulgaris. *Acta Derm Venereol* 2007; 87: 246-54.
28. Pigatto PD, Finzi AF, Altomare GF, Polenghi MM, Vergani C, Vigotti G. Isotretinoin versus minocycline in cystic acne: a study of lipid metabolism. *Dermatologica* 1986; 172: 154-9.
29. Rademaker M, Wishart J m., Birchall N m. Isotretinoin 5 mg daily for low-grade adult acne vulgaris – a placebo-controlled, randomized double-blind study. *Journal of the European Academy of Dermatology and Venereology* 2014; 28: 747-54.
30. Schröder K, Zaun H, Holzmann H, Altmeyer P, el-Gammal S. Pustulosis palmo-plantaris. Clinical and histological changes during etretin (acitretin) therapy. *Acta Derm Venereol Suppl (Stockh)* 1989; 146: 111-6.
31. Schulze HJ, Cribier B, Requena L, Reifenberger J, Ferrández C, García Diez A, et al. Imiquimod 5% cream for the treatment of superficial basal cell carcinoma: results from a randomized vehicle-controlled phase III study in Europe. *Br J Dermatol* 2005; 152: 939-47.
32. Seeberger J, Daoud S, Pammer J. Transient effect of topical treatment of cutaneous leishmaniasis with imiquimod. *Int J Dermatol* 2003; 42: 576-9.
33. Stockfleth E, Meyer T, Benninghoff B, Salasche S, Papadopoulos L, Ulrich C, et al. A randomized, double-blind, vehicle-controlled study to assess 5% imiquimod cream for the treatment of multiple actinic keratoses. *Arch Dermatol* 2002; 138: 1498-502.

34. Swanson N, Smith CC, Kaur M, Goldenberg G. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: two phase 3, multicenter, randomized, double-blind, placebo-controlled studies. *J Drugs Dermatol* 2014; 13: 166-9.
35. Syed TA, Hadi SM, Qureshi ZA, Ali SM, Kwah MS. Treatment of external genital warts in men with imiquimod 2% in cream. A placebo-controlled, double-blind study. *J Infect* 2000; 41: 148-51.
36. Tan J, Humphrey S, Vender R, Barankin B, Gooderham M, Kerrouche N, et al. A treatment for severe nodular acne: a randomized investigator-blinded, controlled, noninferiority trial comparing fixed-dose adapalene/benzoyl peroxide plus doxycycline vs. oral isotretinoin. *Br J Dermatol* 2014; 171: 1508-16.
37. Tanew A, Guggenbichler A, Höningmann H, Geiger JM, Fritsch P. Photochemotherapy for severe psoriasis without or in combination with acitretin: a randomized, double-blind comparison study *J Am Acad Dermatol*. 1991; 25: 682-4.
38. Ulrich C, Bichel J, Euvrard S, Guidi B, Proby CM, van de Kerkhof PCM, et al. Topical immunomodulation under systemic immunosuppression: results of a multicentre, randomized, placebo-controlled safety and efficacy study of imiquimod 5% cream for the treatment of actinic keratoses in kidney, heart, and liver transplant patients. *Br J Dermatol* 2007; 157 Suppl 2: 25-31.
39. Verfaillie CJ, Vanhoutte FP, Blanchet-Bardon C, van Steensel MA, Steijlen PM. Oral liarozole vs. acitretin in the treatment of ichthyosis: a phase II/III multicentre, double-blind, randomized, active-controlled study. *Br J Dermatol* 2007; 156: 965-73.
40. Wu C, Jin HZ, Shu D, Li F, He CX, Qiao J, et al. Efficacy and safety of *Tripterygium wilfordii* hook F versus acitretin in moderate to severe psoriasis vulgaris: a randomized clinical trial. *Chin Med J (Engl)* 2015; 128: 443-9.