Supplementary Online Content

Van Vugt LJ, van den Reek JMPA, Hannink G, Coenen MJH, de Jong EMGJ. Association of *HLA-C*6:02* status with differential response to ustekinumab in patients with psoriasis: a systematic review and meta-analysis. *JAMA Dermatol*. Published online April 17, 2019. doi:10.1001/jamadermatol.2019.0098

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Search Strategy

General search descriptive[a]		
Database searched:		Embase, Medline (including MEDLINE Epub Ahead of Print and In-Process & Other Non-Indexed Citations), Cochrane Library, Web of Science (Web of Science Core Database, SCI-EXPANDED and ESCI)
General search strategy:		Keywords and, when available, MeSH-terms were used to draft up a search strategy combining the following three elements: "psoriasis", "HLA" and "ustekinumab". Synonyms and related terms were used when appropriate.
Limit(s):		Time period: 2016 to present Search conducted on: 14 May 2018 Languages: English, French, German, Dutch
Search software:		Endnote™ X8
Search strings used[b]		
1:	psoriasis	*Psoriasis/* or *Psorias#s.tw.* or *Psorias#s.kf.*
2:	HLA	*HLA-C Antigens/*or *Genes, MHC Class I/*or *(HLA* or human leukocyte antigen* or major histocompatibility complex*).tw.* or *(HLA* or human leukocyte antigen* or major histocompatibility complex*).kf.*
3:	ustekinumab	*interleukin-12/ai* or *interleukin-12 subunit p40/ai* or *interleukin-23/ai* or *(biologic* or ustekinumab or stelara or (anti-IL* adj3 drug*) or (anti-IL* adj3 agent*) or (anti-IL* adj3 therap*) or (anti-IL* adj3 treatment*) or (anti-interleukin* adj3 drug*) or (anti-interleukin* adj3 agent*) or (anti-interleukin* adj3 therap*) or (anti-interleukin* adj3 treatment*) or (IL* adj3 blocker*) or (IL* adj3 blocking agent*) or (IL* adj3 inhibitor*) or (interleukin* adj3 blocker*) or (interleukin* adj3 blocking agent*) or (interleukin* adj3 inhibitor*)).tw.* or *(biologic* or ustekinumab or stelara or (anti-IL* adj3 drug*) or (anti-IL* adj3 agent*) or (anti-IL* adj3 therap*) or (anti-IL* adj3 treatment*) or (anti-interleukin* adj3 drug*) or (anti-interleukin* adj3 agent*) or (anti-interleukin* adj3 therap*) or (anti-interleukin* adj3 treatment*) or (IL* adj3 blocker*) or (IL* adj3 blocking agent*) or (IL* adj3 inhibitor*) or (interleukin* adj3 blocker*) or (interleukin* adj3 blocking agent*) or (interleukin* adj3 inhibitor*)).kf.*
4:	combined search	*#1 and #2 and #3*

[a] Search strings were designed by L.J.v.V. (clinical researcher and PhD student) with support from a medical librarian of the Radboudumc.

[b] The search strings used in Medline are shown; comparable search strings were used for the other databases. Complete search strings are available on request.

eAppendix 2. List of Excluded Articles

1. Akpabio AA, Olaosebikan BH, Adelowo OO. Psoriatic Arthritis in Nigeria: Case Series and Literature Review. *J Clin Rheumatol.* 2018;03:03.
2. Alduraibi F, Omair M, Awwami MA, et al. Prevalence of HLA-B27 in the normal population and patients with axial spondyloarthritis in Saudi Arabia. *Arthritis Rheumatol.* 2016;68:3662-3663.
3. Almodovar R, Batlle E, Collantes E, et al. Checklists (minimun and excellence) for the evaluation of patients with axial spondiyoarthritis in daily practice: Personaliza project. *Ann Rheum Dis.* 2016;75:1146.
4. Anzengruber F. HLA-Cw6 status does not influence the therapy response in psoriasis patients treated with Secukinumab. *Exp Dermatol.* 2018;27 (3):e25-e26.
5. Arends S, Abdulahad W, Boots A, Doornbos-van Der Meer B, Brouwer E, Spoorenberg A. Equal presence of circulating MAIT cells in axial spa patients with only axial involvement and age and sex-matched healthy controls. *Ann Rheum Dis.* 2017;76 (Supplement 2):647.
6. Arun H, Vivek V, Arjun MN, Kunal K, Ramakant S. Clinical Profile of Juvenile Idiopathic Arthritis from a Tertiary Care Centre in North India. *Indian J Rheumatol.* 2017;12 (5 Supplement 1):S103-S104.
7. Aterido A, Julia A, Ferrandiz C, et al. Genome-Wide Pathway Analysis Identifies Genetic Pathways Associated with Psoriasis. *J Invest Dermatol.* 2016;136(3):593-602.
8. Babaie F, Hasankhani M, Mohammadi H, et al. The role of gut microbiota and IL-23/IL-17 pathway in ankylosing spondylitis immunopathogenesis: New insights and updates. *Immunol Lett.* 2018;196:52-62.
9. Bessette L, Kapur S, Zummer M, et al. Predictors of response in patients with ankylosing spondylitis treated with infliximab or golimumab in a real-world setting. *J Rheumatol.* 2016;43 (6):1197.
10. Bojko A, Ostasz R, Bialecka M, et al. IL12B, IL23A, IL23R and HLA-C*06 genetic variants in psoriasis susceptibility and response to treatment. *Hum Immunol.* 2018;79(4):213-217.
11. Borroni RG, Costanzo A. HLA-C*06 and psoriasis: susceptibility, phenotype, course and response to treatment. *Br J Dermatol.* 2018;178(4):825.
12. Brummer GC, Hawkes JE, Duffin KC. Ustekinumab-induced remission of recalcitrant guttate psoriasis: A case series. *JAAD Case Rep.* 2017;3(5):432-435.
13. Burlando M, Cozzani E, Campisi C, di Costanzo A, Parodi A. Different responses to ustekinumab of two HLA-Cw6-positive homozygous twins with psoriasis. *Acta Derm Venereol.* 2016;96(6):858-859.
14. Capon F. The genetic basis of psoriasis. *Int J Mol Sci.* 2017;18 (12) (no pagination)(2526).
15. Chakravadhanula U, Jha B. Remarkable response of recalcitrant hyperkeratotic palmoplantar psoriasis to itolizumab: a case report. *British journal of dermatology Conference: 8th international congress psoriasis from gene to clinic United kingdom.* 2017;177(5):e280-e281. http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/502/CN-01452502/frame.html.
16. Chakravadhanula U, Jha B. Successful treatment of recalcitrant hyperkeratotic palmoplantar psoriasis with itolizumab: a case series of three patients. *British journal of dermatology Conference: 8th international congress psoriasis from gene to clinic United kingdom.* 2017;177(5):e277-e278. http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/504/CN-01452504/frame.html.
17. Chen L, Tsai TF. HLA-Cw6 and psoriasis. *Br J Dermatol.* 2017;26:26.

18. Chung J, Feigenbaum L, Cruz P, Chong B, Ariizumi K. Myeloid-derived suppressor cells (MDSC) in psoriasis are an expanded population with diverse T cell-suppressor mechanisms. *J Invest Dermatol.* 2016;1):S41.
19. Costantino F, Aegerter P, Dougados M, Breban M, D'Agostino MA. Two Phenotypes Are Identified by Cluster Analysis in Early Inflammatory Back Pain Suggestive of Spondyloarthritis: Results From the DESIR Cohort. *Arthritis Rheumatol.* 2016;68(7):1660-1668.
20. Dand N. Genetic variation contributes to response to biologics: Initial findings of the Psoriasis Stratification to Optimise Relevant Therapy (PSORT) consortium. *Br J Dermatol.* 2017;177 (5):e237.
21. Dand N. Psoriasis stratification to optimise relevant therapy (PSORT): Genome-wide study reveals genetic drivers of response to biologic therapy in psoriasis. *J Invest Dermatol.* 2017;137 (10 Supplement 2):S225.
22. Dauden E, Prieto-Perez R, Llamas-Velasco M, Cabaleiro T, Abad-Santos F. Pharmacogenetics of ustekinumab in patients with moderate-to-severe plaque psoriasis. *J Invest Dermatol.* 2016;136 (9 Supplement 2):S188.
23. De Keyser E, Busard C, Coussens E, et al. Therapeutic drug monitoring of ustekinumab in psoriatic patients: Sense or nonsense? *J Eur Acad Dermatol Venereol.* 2016;30:104.
24. Deckers J, Hammad H, Hoste E. Langerhans cells: Sensing the environment in health and disease. *Front Immunol.* 2018;9 (FEB) (no pagination)(93).
25. Derksen N, Niewerth M, Sengler C, et al. Burden of disease, therapy and phenotypes of juvenile psoriatic arthritis-data from the national paediatric rheumatologic database (NPRD) over a 15-year period. *Pediatr Rheumatol.* 2017;15 (Supplement 2):124.
26. Diaz N. American Academy of Dermatology (AAD) - 74thannual meeting Washington, D.C., USA - March 4-8, 2016. *Drugs Future.* 2016;41(4):257-261.
27. Fitzgerald G, Gallagher P, Sullivan C, et al. Dactylitis and enthesitis predict uveitis in large axial spondyloarthropathy cohort. *Arthritis and Rheumatology Conference: American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting, ACR/ARHP.* 2017;69(Supplement 10).
28. Fortin I, Sheriff M, Rahman P, et al. Impact of HLA-b27 on patient profile and treatment response in as patients treated with anti-TNF in Canadian real-world. *Arthritis Rheumatol.* 2016;68:955-957.
29. Furer V, Stark M, Matz H, et al. Prevalence of non-radiographic axial spondyloarthritis in psoriatic arthritis-a single center observational study. *Arthritis Rheumatol.* 2016;68:1234-1235.
30. Furer V, Stark M, Matz H, et al. Whole spine and SIJ MRI of psoriatic arthritis patients: Descriptive study of the spine, and sacroiliac joints involvement in a cross sectional large cohort. *Ann Rheum Dis.* 2017;76 (Supplement 2):747.
31. Galluzzo M, Andreani M, Testi M, Chimenti S, Talamonti M. HLA-C*18:01: A Rare Allele in the European Caucasian Population Coinciding with Difficult-to-Treat Plaque Psoriasis. *Mol Diagn Ther.* 2016;20(3):227-230.
32. Garcia-Porrua C, Mosquera-Martinez JA, Maceiras-Pan FJ, Fernandez-Dominguez L, Guerra-Vazquez L, Pinto-Tasende J. Mixed anxiety-depressive disorder (MADD) in patients with psoriatic arthritis treated with biological therapy. *Ann Rheum Dis.* 2017;76 (Supplement 2):946.

33. Garg T, Sanke S. Inflammatory dermatoses in human immunodeficiency virus. *Indian J Sex Transm Dis.* 2017;38(2):113-120.
34. Generali E, Scire CA, Favalli EG, Selmi C. Biomarkers in psoriatic arthritis: a systematic literature review. *Expert Rev Clin Immunol.* 2016;12(6):651-660.
35. Greb JE, Goldminz AM, Elder JT, et al. Psoriasis. *Nat Rev Dis Primers.* 2016;2 (no pagination)(16082).
36. Gross J, Ramiro S, Etcheto A, et al. Parameters associated with severe axial structural involvement: Data from the bamboo spine cohort on 133 spondyloarthritis patients. *Ann Rheum Dis.* 2016;75:1141.
37. Guarene MM, Cananzi RR, Piccolo AA, et al. Presence of BW4 KIR ligands as a predictive factor of a 'difficult' response to etanercept in moderateto-severe psoriatic patients. *HLA.* 2017;89 (6):474.
38. Hernandez-Baldizon S, Zacarias-Crovato A, Torrente-Segarra V, et al. Characterization of a cohort of psoriatic juvenile idiopathic arthritis patients from a Paediatric University Hospital in Spain. *A Ann Rheum Dis.* 2017;76 (Supplement 2):407.
39. Hong C, Kwan YH, Fong W. Comparison of ankylosing spondylitis and non-radiographic axial spondyloarthritis in a multi-ethnic Asian population of Singapore. *Ann Rheum Dis.* 2017;76 (Supplement 2):918-919.
40. Ikumi K, Kobayashi S, Tamura N, Inoue H, Nishida E, Morita A. HLA-B*46 associates with psoriasis susceptibility. *J Dermatol Sci.* 2017;86 (2):e37.
41. Indhumathi S, Rajappa M, Chandrashekar L, Ananthanarayanan PH, Thappa DM, Negi VS. Pharmacogenetic markers to predict the clinical response to methotrexate in south Indian Tamil patients with psoriasis. *Eur J Clin Pharmacol.* 2017;73(8):965-971.
42. Isidoro-Garcia M, Sanchez-Martin A, Garcia-Berrocal B. Impact of new technologies on pharmacogenomics. *Curr Pharmacogenomics Person Med.* 2016;14(2):74-85.
43. Jadon DR. Psoriatic arthritis and seronegative spondyloarthropathies. *Medicine (United Kingdom).* 2018;46(4):237-242.
44. Ji X, Zhu J, Jianglin, Huang F. Major Clinical characteristics of 831 chinese ankylosing spondylitis patients: Data from a chinese cohort with smart management system for spondyloarthritis. *Int J Rheum Dis.* 2017;20 (Supplement 1):40.
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47. Kim Y. The effect of extraarticular manifestations on tumor necrotic factor alpha inhibitor drug survival in patients with ankylosing spondylitis: Nationwide data from the Korean college of rheumatology biologics (KOBIO) registry. *Arthritis and Rheumatology Conference: American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting, ACR/ARHP.* 2017;69(Supplement 10).
48. Liang Y, Sarkar MK, Tsoi LC, Gudjonsson JE. Psoriasis: a mixed autoimmune and autoinflammatory disease. *Curr Opin Immunol.* 2017;49:1-8.

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50. Litovchenko I, Golovchenko O. The biologic therapy use for enthesitis as a predictor of psoriatic arthritis in psoriatic patients. *Ann Rheum Dis.* 2017;76 (Supplement 2):1321.
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58. Niehues H, Tsoi L, Van Der Krieken D, et al. Psoriasis-associated late cornified envelope proteins have antibacterial activity. *Br J Dermatol.* 2017;177 (5):e236.
59. Niehues H, Tsoi LC, van der Krieken DA, et al. Psoriasis-associated Late Cornified Envelope (LCE) Proteins Have Antibacterial Activity. *J Invest Dermatol.* 2017;17:17.
60. Nikishina I, Kostareva O, Kaleda M, et al. New onset of uveitis, psoriasis or ibd as paradoxical effects of biologics in patients with juvenile idiopathic arthritis: single center experience. *Ann Rheum Dis.* 2017;76 (Supplement 2):1389.
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62. Omar A, Boyd T, Sari I, et al. Acute anterior uveitis in ankylosing spondylitis: Association with inflammatory bowel disease and psoriasis independent of HLA B27. *J Rheumatol.* 2016;43 (6):1172.
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68. Prieto-Perez R, Llamas-Velasco M, Cabaleiro T, et al. Pharmacogenetics of ustekinumab in patients with moderate-to-severe plaque psoriasis. *Pharmacogenomics.* 2017;18(2):157-164.
69. Qiao M, Li R, Zhao X, Yan J, Sun Q. Up-regulated lncRNA-MSX2P1 promotes the growth of IL-22-stimulated keratinocytes by inhibiting miR-6731-5p and activating S100A7. *Exp Cell Res.* 2018.
70. Raine C, Keat A. Axial spondyloarthritis. *Medicine (United Kingdom).* 2018;46(4):231-236.
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73. Schlapbach C, Navarini AA. The continuing evolution of targeted therapy for inflammatory skin disease. *SeminImmunopathol.* 2016;38(1):123-133.
74. Sheng B, Sari I, Alazmi M, Haroon N. Understanding familial ankylosing spondylitis: Clinical characteristics and response to biologics. *J Rheumatol.* 2017;44 (6):857.
75. So A, Anton A, Tsui F, et al. Juvenile-onset ankylosing spondylitis has a lower rate of radiographic progression than adult-onset ankylosing spondylitis. *Arthritis and Rheumatology Conference: American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting, ACR/ARHP.* 2017;69(Supplement 10).
76. Sozeri B, Topaktas E, Kurtulus D. The characteristic of the undifferentiated arthritis in juvenile idiopathic arthritis. *Pediatr Rheumatol.* 2017;15 (Supplement 2):48.
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78. Talamonti M, Galluzzo M, Zangrilli A, et al. HLA-C*06:02 Does Not Predispose to Clinical Response Following Long-Term Adalimumab Treatment in Psoriatic Patients: A Retrospective Cohort Study. *Mol Diagn Ther.* 2017;21(3):295-301.
79. Tanaka Y. Psoriatic arthritis in Japan: Difference in clinical features and approach to precision medicine. *Clin Exp Rheumatol.* 2016;34:1-4.
80. Teo M, Haaland D, Kelsall J, et al. Incidence of extra-articular manifestations in PSA and as patients treated with golimumab in Canadian real-world. *Arthritis and Rheumatology Conference: American*

College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting, ACR/ARHP. 2017;69(Supplement 10).

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84. van den Reek JM, Coenen MJ, van de L'Isle Arias M, et al. Polymorphisms in CD84, IL12B and TNFAIP3 are associated with response to biologics in patients with psoriasis. *Br J Dermatol.* 2016;26:26.
85. van Vugt LJ, van den Reek J, Coenen MJH, de Jong E. A systematic review of pharmacogenetic studies on the response to biologics in psoriasis patients. *Br J Dermatol.* 2017;24:24.
86. Villarreal-Martinez A, Gallardo-Blanco H, Cerda-Flores R, et al. Candidate gene polymorphisms and risk of psoriasis: A pilot study. *Exp Ther Med.* 2016;11(4):1217-1222.
87. Von Brandis E. Juvenile spondyloarthritis (JSpA). *Pediatr Radiol.* 2017;47:S320-S321.
88. Wang WM, Jin HZ. Homocysteine: A potential common route for cardiovascular risk and DNA methylation in psoriasis. *Chin Med J.* 2017;130(16):1980-1986.
89. Wendling D, Guillot X, Gossec L, Prati C, Saraux A, Dougados M. ASDAS-based remission was less frequent than basdai-based remission, and both were related to CRP and smoking in early axial spondyloarthritis. The DESIR cohort. *Ann Rheum Dis.* 2016;75:323.
90. Witoelar A, Jansen IE, Wang Y, et al. Genome-wide Pleiotropy Between Parkinson Disease and Autoimmune Diseases. *JAMA Neurol.* 2017;74(7):780-792.
91. Yamamoto T, Kawada A. Clinical characteristics of Japanese patients with psoriatic arthritis: Comparison with East Asian countries. *J Dermatol.* 2018;45(3):273-278.
92. Yamamoto T, Ohtsuki M, Sano S, et al. Epidemiological analysis of psoriatic arthritis patients in Japan. *J Dermatol.* 2016;43(10):1193-1196.
93. Yarkan H, Li Z, Kenar G, et al. Phenotype differences in HLA-b27 positive versus negative patients with ankylosing spondylitis in a population that show relatively weaker association with hla-b27. *Arthritis and Rheumatology Conference: American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting, ACR/ARHP*. 2017;69(Supplement 10).
94. Zhang X. Advances in genomic studies of psoriasis in China. *Br J Dermatol.* 2017;177 (5):e240-e241.
95. Ziade NR, Fayad F, Mallak I, Merheb G, Witte T, Baraliakos X. Anti-CD74 antibodies: Diagnostic properties in low HLA-B27 early axial spondyloarthritis. *Ann Rheum Dis.* 2017;76 (Supplement 2):667.

eAppendix 3. Gray Literature Search OpenGrey.eu

General search descriptive	
Source:	OpenGrey.eu
Search date:	4 June 2018
Number of hits:	8 hits; none relevant
Search strategy:	*(psoriasis pharmacogen*)* and *(psoriasis human leukocyte antigen*)* and *(psoriasis HLA*)* and *(psoriasis ustekinumab)*

List of hits

1. Phenotypical and functional study of the regulatory T cells in patients affected by psoriasis: modifications observed under treatment with TNF alpha blocking agent (Infliximab); Arsouze, Amélie; 2007; Thesis (Ph.D.); Université Pierre et Marie Curie, UFR de médecine Pierre et Marie Curie, Paris; France.
2. The Potential of Pharmacogenetics to Optimise Methotrexate use for Psoriasis; Warren, Richard Bruce; 2008; Thesis (Ph.D.); University of Manchester; United Kingdom.
3. Traitement par anti-TNFa de 203 formes axiales de spondylarthropathies (profil des patients, et réponse à 6 mois en fonction de la satisfaction ou non des critères de New York et des recommandations françaises pour l'instauration de ces traitements); Gerard Benoist, Stéphanie; 2008; Thesis (Ph.D.); Université de Nantes, Unité de Formation et de Recherche de Médecine et des Techniques Médicales; France.
4. Recherche de gènes de prédisposition à une maladie à hérédité complexe (le psoriasis); Oudot, Tiphaine; 2009; Thesis (Ph.D.); Université d'Évry-Val-d'Essonne; France.
5. Imputation aided analysis of the association between autoimmune diseases and the MHC; Moutsianas, Loukas; 2011; Thesis (Ph.D.); University of Oxford; United Kingdom.
6. New biotherapies in psoriasis; Ngo Thanh, Claire; 2011; Thesis (Ph.D.); Université Paul Sabatier, Toulouse ; Université Paul Sabatier, Faculté des sciences pharmaceutiques, Toulouse; France.
7. Place de l'Ustekinumab, un anticorps monoclonal dirigé contre la chaîne p40 commune aux interleukines IL-12 et IL-23, dans le traitement du psoriasis; Cart, Sophie; 2012; Thesis (Ph.D.); Université de Franche-Comté, Faculté de médecine et de pharmacie; France.
8. Genetics of ankylosing spondylitis; Karaderi, Tugce; 2012; Thesis (Ph.D.); University of Oxford; United Kingdom.

eAppendix 4. Gray Literature Search ClinicalTrials.gov

General search descriptive	
Source:	ClinicalTrials.gov
Search date:	4 June 2018
Number of hits:	59 hits; none relevant
Search strategy:	*Disease:* psoriasis *Intervention:* ustekinumab

List of hits

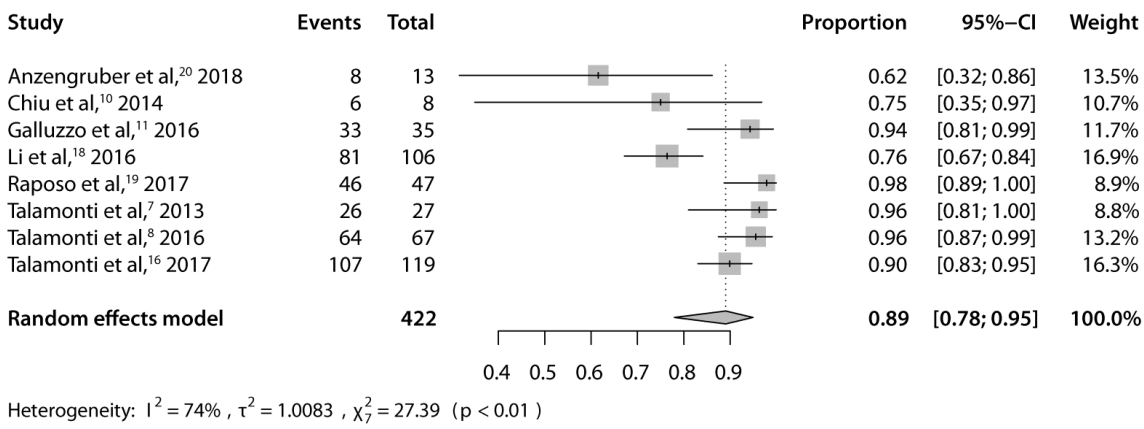
1. NCT02698475; An Efficacy, Safety, and Pharmacokinetics Study of Subcutaneously Administered Ustekinumab in the Treatment of Moderate to Severe Chronic Plaque Psoriasis in Pediatric Participants Greater Than or Equal to 6 to Less Than 12 Years of Age.
2. NCT03218488; A Safety Study of Ustekinumab in the Treatment of Pediatric Participants Aged 12 Years and Older With Moderate to Severe Plaque Psoriasis.
3. NCT01999868; Efficacy of Ustekinumab Followed by Abatacept for the Treatment of Psoriasis Vulgaris.
4. NCT01511315; Quality of Life Study in Psoriasis Patients After Ustekinumab Treatment.
5. NCT02826603; Study of Secukinumab Compared to Ustekinumab in Subjects With Plaque Psoriasis.
6. NCT00267969; A Study of Safety and Effectiveness of Ustekinumab (CNTO 1275) in Patients With Moderate to Severe Plaque-type Psoriasis.
7. NCT02693470; The Difference of Microparticles in Patients With Psoriasis Vulgaris Who Received Stelara (Ustekinumab).
8. NCT01276847; A Study to Assess the Effect of Ustekinumab (Stelara®) and Etanercept (Enbrel®) in Participants With Moderate to Severe Psoriasis (MK-0000-206).
9. NCT01090063; Efficacy and Safety of Ustekinumab in Patients With Moderate to Severe Palmar Plantar Psoriasis.
10. NCT00320216; A Safety and Effectiveness Study of CNTO 1275 in Patients With Moderate to Severe Plaque-type Psoriasis.
11. NCT01090427; A Study of the Safety and Efficacy of Ustekinumab in Adolescent Patients With Psoriasis (CADMUS).
12. NCT01091051; Safety and Efficacy of Ustekinumab in Patients With Palmo-Plantar Pustular Psoriasis or With Palmo-Plantar Pustulosis.
13. NCT01677598; A Study to Evaluate Ustekinumab in Patients With Plaque Psoriasis in Asia-Pacific Countries.

14. NCT01059773; A Safety and Efficacy Study of Ustekinumab in Patients With Plaque Psoriasis Who Have Had an Inadequate Response to Methotrexate.
15. NCT02074982; Efficacy of Secukinumab Compared to Ustekinumab in Patients With Plaque-type Psoriasis.
16. NCT01558310; A Study to Evaluate the Effectiveness of STELARA ™ (USTEKINUMAB) in the Treatment of Scalp Psoriasis.
17. NCT00747344; A Phase 3 Trial to Look at the Safety and Effectiveness of Ustekinumab in Korean and Taiwanese Subjects With Moderate to Severe Plaque-type Psoriasis.
18. NCT02203032; A Study of Guselkumab in Participants With Moderate to Severe Plaque-type Psoriasis and an Inadequate Response to Ustekinumab.
19. NCT00307437; A Study of the Safety and Efficacy of Ustekinumab (CNTO 1275) in Patients With Moderate to Severe Psoriasis.
20. NCT02684370; BI 655066 (Risankizumab) Compared to Placebo and Active Comparator (Ustekinumab) in Patients With Moderate to Severe Chronic Plaque Psoriasis.
21. NCT01008995; A Study of the Safety and Effectiveness of Ustekinumab (Stelara) in Chinese Patients With Psoriasis.
22. NCT02684357; BI 655066 Compared to Placebo & Active Comparator (Ustekinumab) in Patients With Moderate to Severe Chronic Plaque Psoriasis.
23. NCT02187172; Vascular Inflammation in Psoriasis-Ustekinumab (VIP-U).
24. NCT02561806A; A Study of Ixekizumab (LY2439821) in Participants With Moderate-to-Severe Plaque Psoriasis.
25. NCT00723528; An Efficacy and Safety Study of Ustekinumab (CNTO 1275) in Participants With Plaque Psoriasis.
26. NCT01550744; A Study of Ustekinumab to Evaluate a "Subject-tailored" Maintenance Dosing Approach in Subjects With Moderate-to-Severe Plaque Psoriasis.
27. NCT00454584; An Efficacy and Safety Study of CNTO 1275 Compared to Etanercept in Patients With Plaque Psoriasis.
28. NCT01708629; Study of Efficacy and Safety of Brodalumab Compared With Placebo and Ustekinumab in Moderate to Severe Plaque Psoriasis Subjects.
29. NCT01708603; Study of Efficacy and Safety of Brodalumab Compared With Placebo and Ustekinumab in Moderate to Severe Plaque Psoriasis Subjects.
30. NCT02054481; BI 655066 Dose Ranging in Psoriasis, Active Comparator Ustekinumab.
31. NCT02786732; Study to Evaluate Broadlumab vs Placebo and Ustekinumab.
32. NCT00870285; Ustekinumab Plus UVB-311nm in Psoriasis.
33. NCT03370133; A Study to Evaluate the Efficacy and Safety of Bimekizumab Compared to Placebo and an Active Comparator in Adult Subjects With Moderate to Severe Chronic Plaque Psoriasis.
34. NCT01081730; Ustekinumab Safety and Surveillance Program Using the Ingenix NHI Database.
35. NCT02144857; Effects of Treatment With Biological Agents on Vascular and Cardiac Function in Psoriasis.

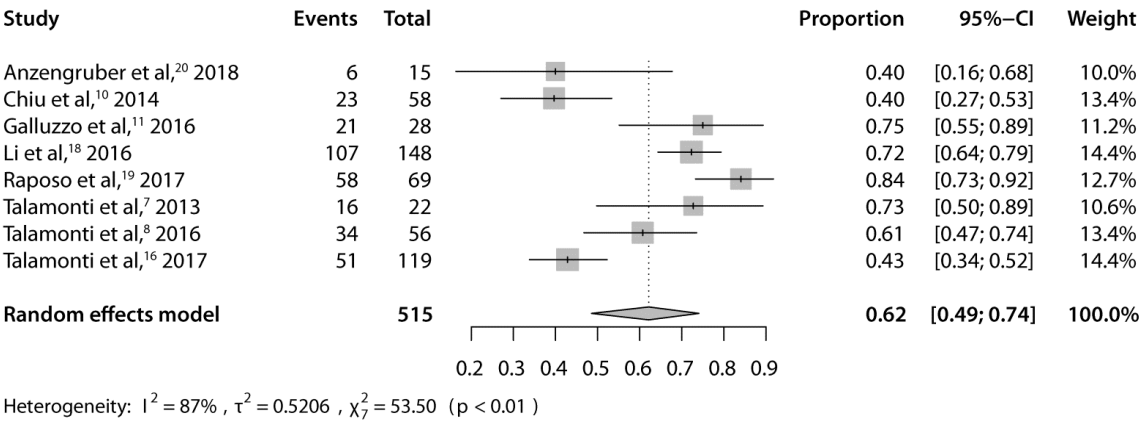
36. NCT00508547; Psoriasis Longitudinal Assessment and Registry (PSOLAR).
37. NCT02075697; Spanish Registry of Systemic Treatments in Psoriasis.
38. NCT01706692; Swiss Dermatology Network of Targeted Therapies (SDNTT).
39. NCT03358693; Anti-cytokine Signatures in Inflammatory Skin Disease.
40. NCT01848028; PsoBest - The German Psoriasis Registry.
41. NCT02763969; Safety Study of BMS-986202 in Healthy Subjects and to Treat Psoriasis.
42. NCT02103361; Stelara Pregnancy Exposure Registry OTIS Autoimmune Diseases in Pregnancy Project.
43. NCT03148860; Impact of Concomitant MTX on Efficacy, Safety and Adherence of Ustekinumab-treatment in Patients With Active PsA.
44. NCT02330380; Comparative Effectiveness of Psoriasis Treatments on Systemic Inflammation.
45. NCT01356758; Cardiovascular Risk Assessment in Patients With Severe Psoriasis Treated With Biologic Agents.
46. NCT01812954; Economic Evaluation of Systemic Treatments for Moderate-to-severe Psoriasis.
47. NCT02602925; Tight Control Dose Reductions of Biologics in Psoriasis Patients With Low Disease Activity.
48. NCT01903317; Evaluation of Vitamin D Levels in Psoriasis Patients.
49. NCT01009086; A Study of the Safety and Effectiveness of Ustekinumab in Patients With Psoriatic Arthritis.
50. NCT01077362; A Study of the Safety and Efficacy of Ustekinumab in Patients With Psoriatic Arthritis With and Without Prior Exposure to Anti-TNF Agents.
51. NCT03336281; A Study to Characterize Profile of Participant With Psoriatic Arthritis Depending on Whether Their Disease is Managed by a Dermatologist or by a Rheumatologist, and Starting Ustekinumab.
52. NCT02627768; A Study on Assessment of STELARA and Tumor Necrosis Factor Alpha Inhibitor Therapies in Participants With Psoriatic Arthritis.
53. NCT00267956; An Effectiveness and Safety Study of CNTO 1275 in Patients With Active Psoriatic Arthritis.
54. NCT02319759; Efficacy and Safety Study of Guselkumab in the Treatment of Participants With Active Psoriatic Arthritis (PsA).
55. NCT01965132; Korean College of Rheumatology Biologics Registry.
56. NCT03006198; Tracking Biologics Along the Silk Road.
57. NCT00741793; Biologic Treatment Registry Across Canada.
58. NCT03465696; A Priming Intervention to Increase Patient Willingness to Use Injectables for the Management of Psoriasis.
59. NCT03496831; Predicting Hospitalized Infection in Patients With Chronic Inflammatory Arthritis Treated With Biological Drugs.

eFigure 1. Pooled Proportions for Response Rates at 6 Months for *HLA-C*06:02*–positive (A) and *HLA-C*06:02*–negative (B) Patients Treated With Ustekinumab

(A)

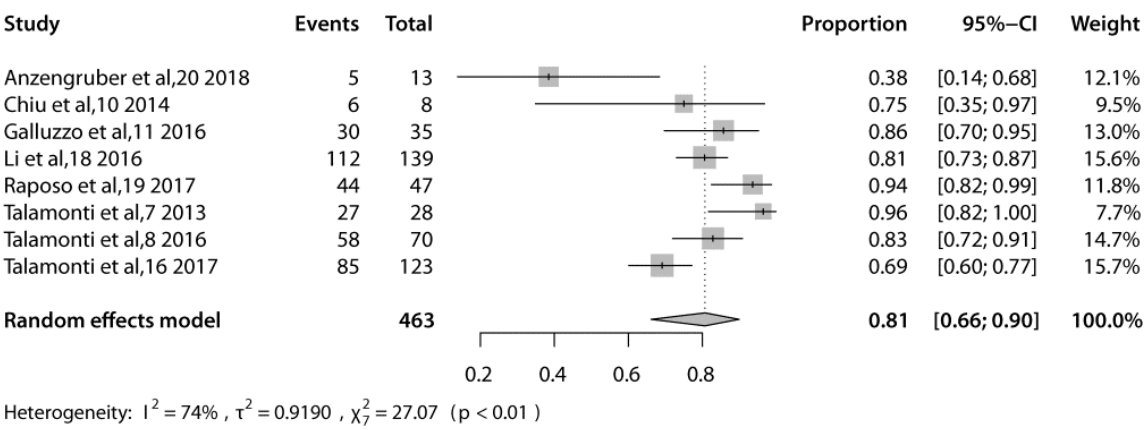


(B)

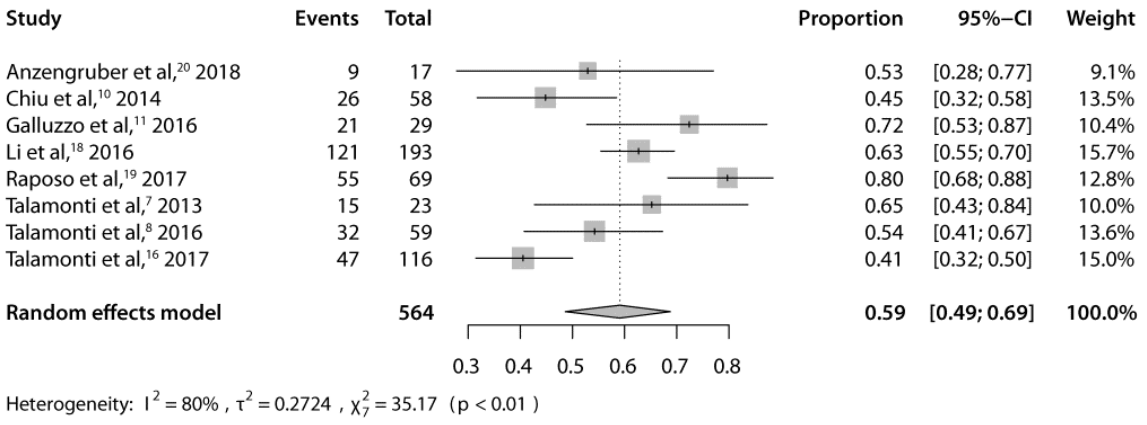


eFigure 2. Pooled Proportions for Response Rates at 3 Months for *HLA-C*06:02*–positive (A) and *HLA-C*06:02*–negative (B) Patients Treated With Ustekinumab

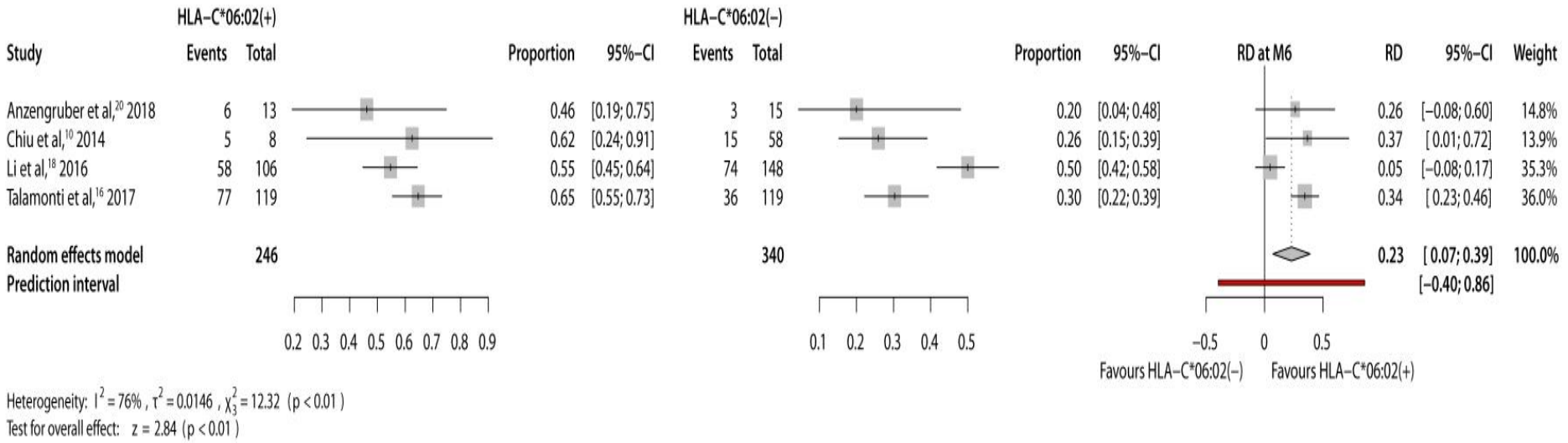
(A)



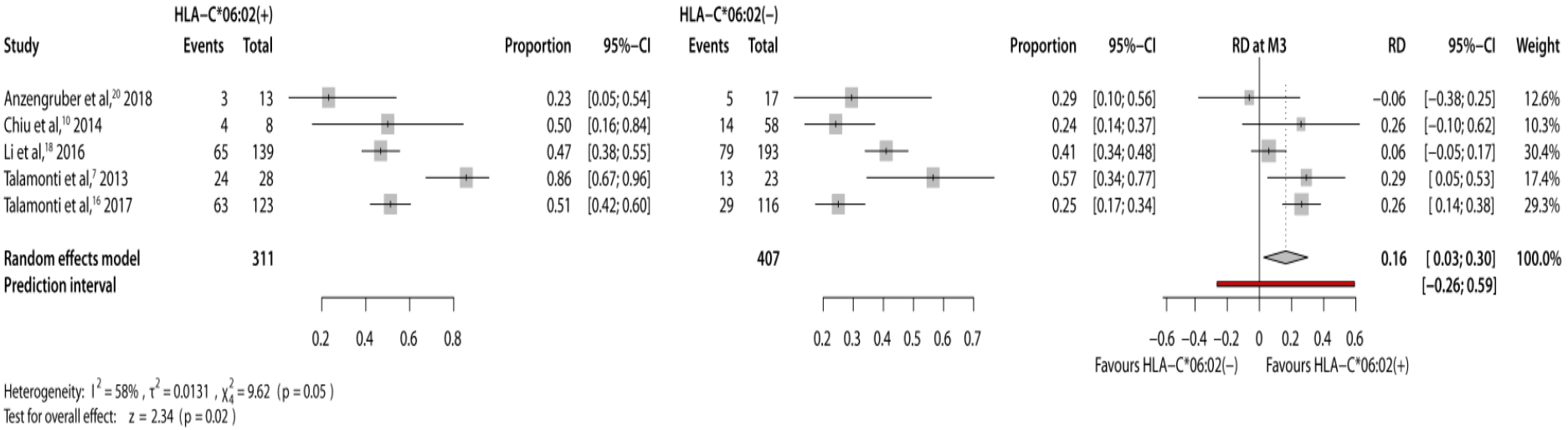
(B)



eFigure 3. Risk Difference for Response to Ustekinumab (PASI90) at 6 Months' Treatment According to *HLA-C*06:02* Status

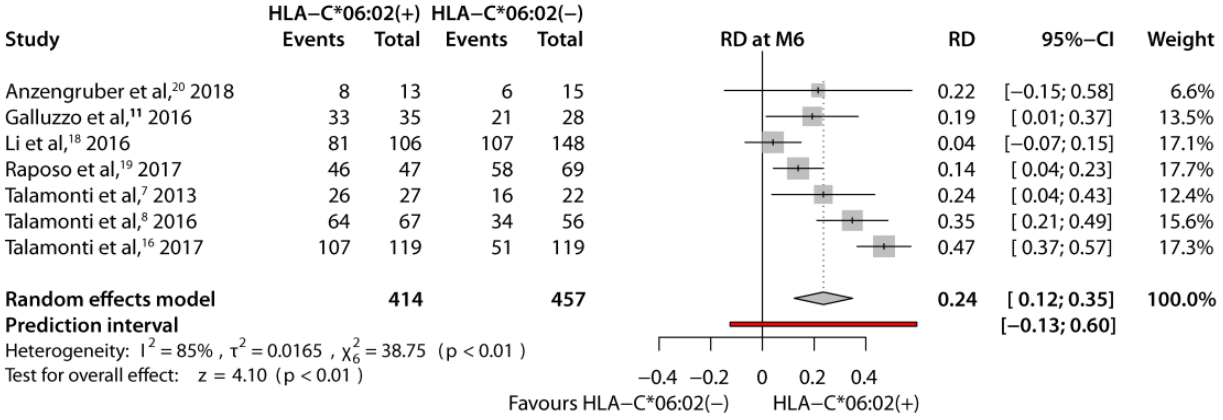


eFigure 4. Risk Difference for Response to Ustekinumab (PASI90) at 3 Months' Treatment According to *HLA-C*06:02* Status



Heterogeneity: $I^2 = 58\%$, $\tau^2 = 0.0131$, $\chi^2_4 = 9.62$ ($p = 0.05$)
Test for overall effect: $z = 2.34$ ($p = 0.02$)

eFigure 5. Sensitivity Analysis Based on Exclusion of Non-European/Non-North American Cohorts

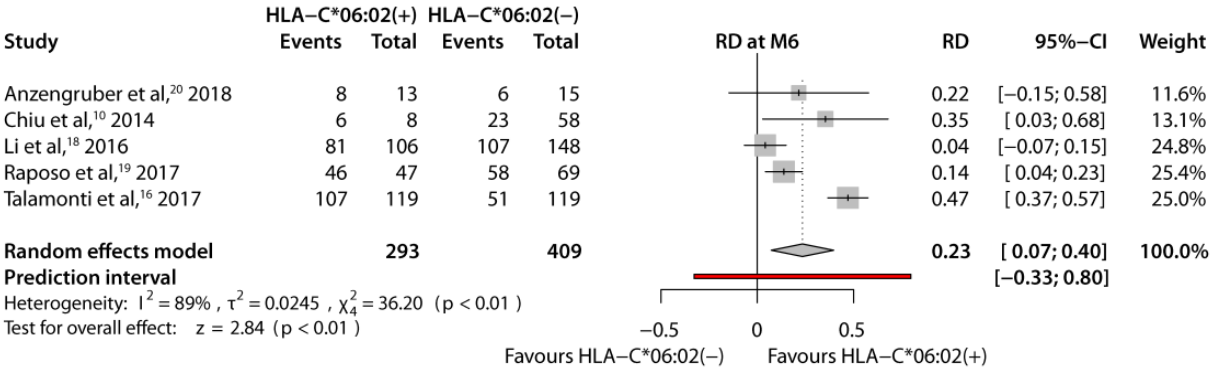


Abbreviations: M6, six months; RD, risk difference.

Exclusion of Non-European/Non-North American cohorts

Ethnicity is an important possible confounder in genetic studies.[27,28] Therefore, a sensitivity analysis based on ethnic groups would be desirable. Unfortunately, only three out of eight included studies (*Talamonti et al.* 2016*, Chiu et al.* and *Li et al.*) reported on ethnicity of their study population. In other studies, ethnicity of the included patients was not explicitly reported. Performing a sensitivity analysis based on ethnicity was therefore not feasible. Instead, we have performed a sensitivity analysis based on geographic area as a proxy for ethnicity. For this analysis, we included all European and all North American studies, meaning that only the cohort of *Chiu et al.* (study performed in Asia) was excluded.

eFigure 6. Sensitivity Analysis Based on Exclusion of Same Research Groups

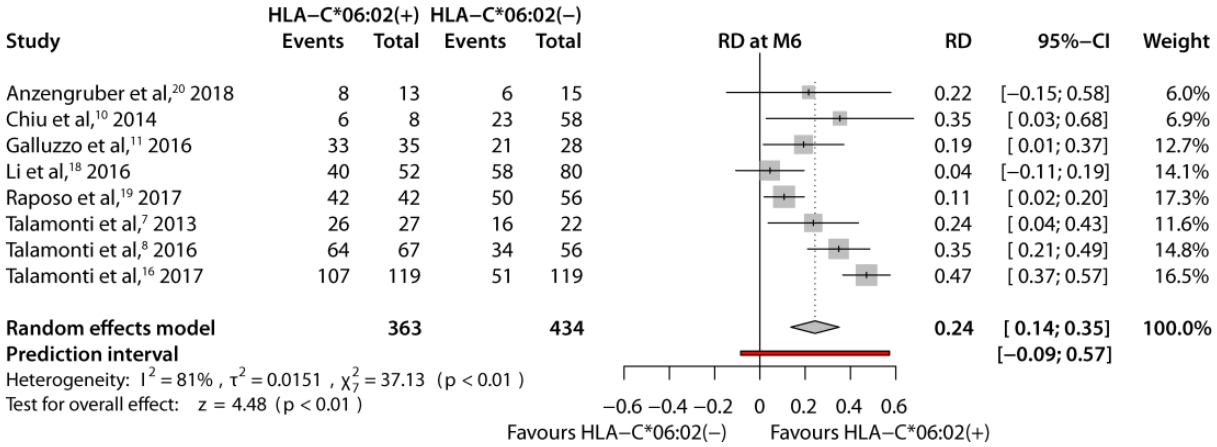


Abbreviations: M6, six months; RD, risk difference.

Exclusion of same research groups

For our primary analysis, studies containing duplicate data (same patients being represented in more than one publication) were excluded. We refer to the relevant sections of 'Materials and Methods' and 'Results' for a more detailed discussion of this process. Although our primary analyses did not contain duplicate data, four out of eight included studies were published by the same research group (*Talamonti et al./Galluzzo et al.* from Rome, Italy). Multiple cohorts from one research group and location may shift results into a certain direction. Therefore, we performed a sensitivity analysis where three out of four publications by *Talamonti et al./Galluzzo et al.* were excluded, leaving only the most recent publication (*Talamonti 2017*).

eFigure 7. Sensitivity Analysis Based on Exclusion of Non-according-to-label Dosing

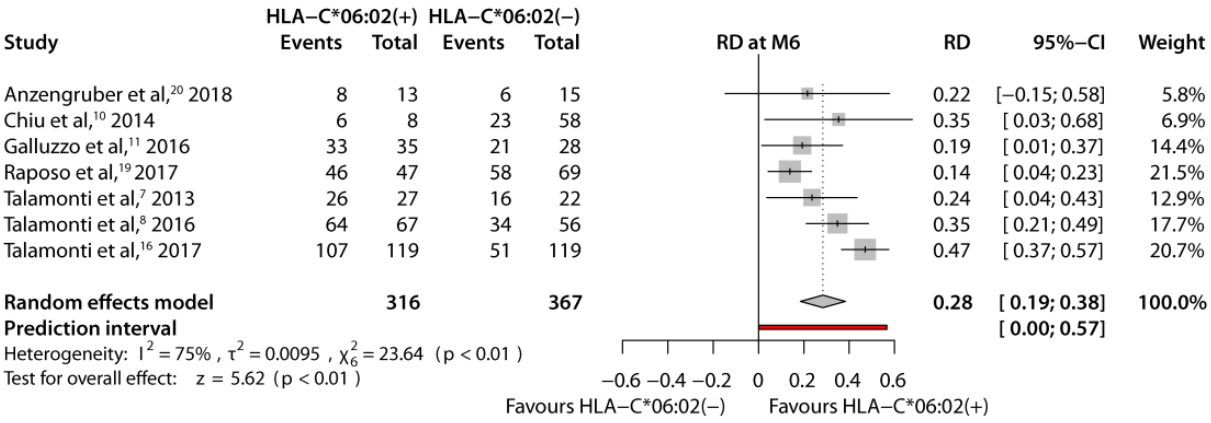


Abbreviations: M6, six months; RD, risk difference.

Exclusion of non-according-to-label dosing

The label for ustekinumab recommends a dose of 45 mg for patients weighing ≤100 kg, and 90 mg for patients >100 kg, to be administered subcutaneously at week 0, week 4 and then every 12 weeks thereafter. For the seven daily practice studies, according-to-label-dosing was explicitly mentioned in five of the papers (*Anzengruber*, *Galluzzo*, *Talamonti 2013*, *Talamonti 2016*, *Talamonti 2017*). In the article by *Chiu et al.* a regimen of 45 mg at week 0, 4 and then every 12 weeks was reported, without any mention of weight-based dosing. A mean weight of 73 kg in their population (SD 14.5) suggests that nearly all of their patients were in fact <100 kg of weight. In the RCTs included by *Li et al.*, patients were randomized to 45 or 90 mg of ustekinumab regardless of their weight, meaning that about half of patients were treated with a non-according-to-label dose (45 mg for patients >100 kg or 90 mg for patients ≤100 kg). Contact with *Raposo et al.* revealed that all patients started treatment according-to-label, but dose adjustments were made during the first six months of treatment in a part of the cohort. As a sensitivity analysis, we excluded all patients who received a non-according-to-label dose in the study by *Li et al*. (123 of 255 patients excluded), and all patients who received dose adjustments in the study by *Raposo et al.* (18 of 116 patients excluded). This led to a pooled RD of 0.24 at six months (95% CI: 0.14-0.34).

eFigure 8. Sensitivity Analysis Based on Exclusion of Randomized Clinical Trials



Abbreviations: M6, six months; RD, risk difference.

Exclusion of randomized clinical trials

Randomized clinical trials reflect treatment in a highly controlled, optimal setting where confounders are reduced to a minimum.[31,32] Strict inclusion criteria and controlled conditions make for a homogenous cohort, both in terms of patient characteristics and in treatment received. This sharply contrasts daily practice cohorts, which may be (highly) heterogeneous in both aspects.[31,32] To assess the influence of study design (observational versus RCT), we performed a sensitivity analysis excluding the study by *Li et al.* which was the only study based on RCT data.

eTable. Risk of Bias Assessment

Reference	Selection				Comparability		Outcome			Quality judgment
	S1[a]	S2	S3	S4[b]	C1[c]	C2[d]	O1	O2[e]	O3[f]	
Anzengruber et al. (2018)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆
Chiu et al. (2014)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆
Galluzzo et al. (2016)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆
Li et al. (2016)	★	★	★	n/a	★	-	★	★	-	★★★★★★☆☆
Raposo et al. (2017)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆
Talamonti et al. (2013)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆
Talamonti et al. (2016)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆
Talamonti et al. (2017)	★	★	★	n/a	-	-	★	★	★	★★★★★★☆☆

Abbreviations: S1, Representativeness of the exposed cohort; S2, Selection of the non-exposed cohort; S3, Ascertainment of exposure; S4, Demonstration that outcome of interest was not present at start of study; C1/C2, Comparability of cohorts on the basis of the design or analysis; O1, Assessment of outcome; O2, Was follow-up long enough for outcomes to occur; O3, Adequacy of follow-up of cohorts.

References: *Anzengruber et al.* (2018)[20], *Chiu et al.* (2014)[10], *Galluzzo et al.* (2016)[11], *Li et al.* (2016)[18], *Raposo et al.* (2017)[19], *Talamonti et al.* (2013)[7], *Talamonti et al.* (2016)[8], *Talamonti et al.* (2017)[16]. NB: Additional data provided by the authors (e.g. regarding follow-up) was also taken into account when performing the NOS scoring.

[a] Patients with moderate-to-severe psoriasis who are eligible for biologic treatment.

[b] Outcome of interest in context would be achievement of PASI75 after six months, yes or no. Answering 'yes' to this question would in this case require patients to be included for the pharmacogenetics study at baseline, instead of retrospectively (when response status was already known). However, retrospective assessment of genotype status may actually, in theory, lead to a *lower* chance of bias, because PASI assessment could then not be influenced by known genotype status. Because of this contradiction, we determined that the attribution of answering this question (S4) with respect to actual risk of bias assessment is unclear. We therefore decided to omit S4.

[c] Study adequately controls for ethnicity.

[d] Study adequately controls for other possible confounders/covariates, or, analyses ruling out possible confounders were performed.

[e] Twenty-four weeks or longer was regarded a sufficient follow-up period.

[f] A follow-up rate of >90% was regarded as adequate.

eReferences

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