ORIGINAL ARTICLE

Response to IL-17A inhibitors secukinumab and ixekizumab cannot be explained by genetic variation in the protein-coding and untranslated regions of the IL-17A gene: results from a multicentre study of four European psoriasis cohorts

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Abstract

Background Genetic predictors for treatment response could optimize allocation of biological treatment in patients with psoriasis. There is minimal knowledge about pharmacogenetics of anti-IL-17 agents.

Objectives To assess whether genetic variants in the protein-coding region or untranslated regions of the *IL-17A* gene are associated with response to IL-17A inhibitors in patients with psoriasis.

Methods This was a multicenter European cohort study investigating pharmacogenetics of IL-17A inhibitors in patients with psoriasis. Patients with plaque psoriasis treated with secukinumab or ixekizumab in daily practice were included. For all participants, the protein-coding region and untranslated regions of the *IL-17A* gene were analysed using Sanger sequencing. Identified genetic variants were tested for association with response to secukinumab/ixekizumab, measured as ΔPASI, after 12 weeks (primary outcome) and after 24 weeks (secondary outcome). Association was tested using a linear regression model with correction for baseline PASI as a fixed covariate and for biological naivety and body mass index as additional covariates.

Results In total, 134 patients treated with secukinumab or ixekizumab were included. Genotyping of the cohort identified genetic variants present in untranslated regions and intronic DNA, but not in the protein-coding region of the *IL-17A* gene. Five genetic variants in non-coding DNA with a known or suspected functional effect on IL-17A expression were selected for association analyses: rs2275913, rs8193037, rs3819025, rs7747909 and rs3748067. After 12 weeks, 62% of patients achieved PASI75 and 39% achieved PASI90. At week 24, PASI75 and PASI90 response rates were 72% and 62%, respectively. No associations were found between the five genetic variants and ΔPASI, PASI75 or PASI90 after 12 and 24 weeks of anti-IL-17A treatment.

Conclusions Response to IL-17A inhibitors secukinumab and ixekizumab cannot be explained by genetic variation in the protein-coding and untranslated regions of the *IL-17A* gene. Pharmacogenetics of IL-17A inhibitors in the treatment of psoriasis requires further exploration.

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Conflicts of interest

L.J. van Vugt carries out clinical trials for AbbVie, Celgene, Janssen and Novartis. All funding is not personal but goes to the independent research fund of the department of dermatology of Radboud University Medical Centre Nijmegen, the Netherlands. J.M.P.A. van den Reek carries out clinical trials for AbbVie, Celgene and Janssen; has received speaking fees from AbbVie and Janssen; and has received reimbursement for attending a symposium from Celgene and AbbVie. All funding is not personal but goes to the independent research fund of

the department of dermatology of Radboud University Medical Centre Nijmegen, the Netherlands. K. Kingo served as a principal investigator in clinical studies sponsored by Celgene, Mitsubishi Pharma, Novartis, Merck, Regeneron and Sandoz. J. Lambert has received unrestricted grants from AbbVie, Celgene, Eli-Lilly, Janssen-Cilag, LEO Pharma and Novartis; has been a speaker for Pfizer, AbbVie, and Janssen-Cilag; and has served as a consultant for AbbVie, Celgene, Eli-Lilly, Janssen-Cilag, LEO Pharma and Novartis. All funding is not personal but goes to the independent research fund of the Department of Dermatology, Ghent University Hospital, Belgium. E.M.G.J. de Jong has received research grants for the independent research fund of the department of dermatology of the Radboud University Medical Centre Nijmegen, the Netherlands from AbbVie, Pfizer, and Janssen Pharmaceutica; has acted as consultant and/or paid speaker for; and/or participated in research sponsored by companies that manufacture drugs used for the treatment of psoriasis including AbbVie, Janssen Pharmaceutica, Novartis, Lily, Celgene and Leo Pharma. All funding is not personal but goes to the independent research fund of the Department of Dermatology of Radboud University Medical Centre Nijmegen, the Netherlands. E. Meulewaeter, M. Hakobjan, N. Heddes, T. Traks, M. Galluzzo, M. Talamonti, M.J.H. Coenen have no conflicts of interest to declare.

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Introduction

Psoriasis vulgaris is a chronic, immune-mediated skin disease with an estimated prevalence of 2% in Europe and the United States.[1] For patients with moderate-to-severe disease, systemic therapy is often indicated.[2] Biologicals are systemic agents targeting specific cytokines involved in psoriasis pathogenesis. Nowadays, a variety of biological therapies are available for psoriasis patients. These agents are potentially highly effective[3]; however, treatment costs are considerable and the response is variable between patients. Finding biomarkers to predict treatment response is therefore high on the research agenda.

Genetic variants may explain part of the observed variability in treatment response and serve as biomarkers for treatment success, a field known as pharmacogenetics.[4] For psoriasis, pharmacogenetics research of the last decade has mostly focused on identification of genetic markers predicting response to the various biological agents. In a systematic review on this topic, we found that current knowledge is limited mainly to TNF blockers (etanercept, infliximab, adalimumab) and the IL-12/23 inhibitor ustekinumab.[5] A newer class of biologicals, targeting the IL-17 cytokine, became available for treatment of plaque psoriasis in 2015. Agents within this class are secukinumab and ixekizumab (both IL-17A inhibitors) and brodalumab (an IL-17-receptor blocker).[6–8] Studies investigating pharmacogenetics of IL-17 inhibitors are scarce. Recently, Costanzo *et al.*[9] published results of the SUPREME study, investigating the effect of *HLA-C*06:02* status in patients treated with the IL-17A inhibitor secukinumab in a trial setting. They found no influence of *HLA-C*06:02* status on PASI90 response rates after 16 weeks of treatment.[9] Likewise, Anzengruber *et al.*[10] found that *HLA-C*06:02* status did not influence response to secukinumab in a small cohort of psoriasis patients treated in daily practice. Additional studies on this topic are needed to move a step closer towards genetics-based treatment allocation in psoriasis.

Secukinumab and ixekizumab are monoclonal antibodies targeting IL-17A, with ixekizumab also binding to the heterodimer form of the protein (IL-17A/F).[6,7] We hypothesized that genetic variants in the protein-coding and surrounding regions of the *IL-17A* gene could lead to changes in expression or function of the IL-17A protein, influencing effectiveness of IL-17A inhibiting drugs. To investigate this hypothesis, we sequenced the protein-coding region and untranslated regions important for the expression of the *IL-17A* gene, in patients with psoriasis treated with secukinumab or ixekizumab in daily practice. Identified genetic variants were tested for association with treatment response at 12 and 24 weeks.

Materials and methods

We performed a multicentre study, investigating association between genetic variants in the *IL-17A* gene and clinical response to IL-17A inhibitors in patients with psoriasis. Data were provided by four European university hospitals: Radboud University Medical Centre (Radboudumc) in Nijmegen, the Netherlands; University Hospital Ghent in Ghent, Belgium; University of Rome Tor Vergata in Rome, Italy; and University of Tartu in Tartu, Estonia. This study was approved by the local ethics committee of the Radboudumc. All participants gave informed consent.

Patients

Patients with plaque psoriasis who were treated with secukinumab or ixekizumab in daily practice between 2015 and 2018 were eligible for inclusion. Previous use of secukinumab or ixekizumab in a clinical trial was considered an exclusion criterion.

Patients who were treated with an IL-17A inhibitor primarily for psoriatic arthritis were also excluded.

Data collection

Venous blood for genotyping was collected in ethylenediaminetriacetic acid (EDTA) tubes and stored below −70°C. Clinical data were collected anonymously from all participating centres using Castor EDC.[11] Collected data included baseline demographics, treatment received and Psoriasis Area and Severity Index (PASI) scores during the first 6 months of treatment.

DNA extraction and genotyping

DNA was extracted from whole blood using standard methods (e.g. QIAamp DNA Blood Midi Kit from Qiagen, Hilden, Germany). DNA quality and integrity were checked before genotyping. Primers were designed to capture all three exons of the *IL-17A* gene, including a margin of 20 base pairs from both the intron–exon and exon–intron junctions. For the first exon, a longer upstream sequence from the intron–exon junction was chosen (200 base pairs) to also capture rs2275913 – a SNP with known functional effects on *IL-17A* gene expression[12–16] that has been associated with various autoimmune diseases,[17] and also with clinical response to TNF blockers in some of these diseases.[18,19] Forward and reverse primer sequences are shown in Table S1. Genomic DNA (10 ng) was amplified using AmpliTaq Gold 360 Master Mix (Applied Biosystems, Foster City, California, United States), with 0.3 μmol/L forward and the same amount of reverse primer. PCR amplification was performed using an annealing temperature of 57°C. PCR products were purified with FastAP Thermosensitive Alkaline Phosphatase and Exonuclease I (Thermo Fisher Scientific, Waltham, MA, USA) and the *IL-17A* gene was Sanger sequenced, using the PCR primers described previously. Sequence results were analysed using Vector NTI software from Thermo Fisher Scientific.

Statistical analyses

For the pharmacogenetics analyses, all variants found in protein-coding regions of *IL-17A* were included. For variants found in non-coding regions, only those with a known or suspected functional effect were included for further analyses. Hardy–Weinberg equilibrium was evaluated using chi-square tests.

For all included variants, association with clinical response to the IL-17A inhibitor (secukinumab or ixekizumab) was assessed. Clinical response was measured by absolute changes in PASI scores compared to baseline (ΔPASI) at two time points: after 12 weeks (primary outcome) and after 24 weeks (secondary outcome). PASI scores for week 12 and week 24 were obtained by interpolating between scores of the most nearby visits, using a maximum of 180 days between two PASI measures to allow interpolation. When interpolation was not possible, PASI measurements made within 30 days of the week 12 or week 24 time point were used. When no nearby measurement was available either, the follow-up PASI was recorded as missing.

Influence of genetic variants on ΔPASI was evaluated by single-variant testing, using a linear regression model with correction for baseline PASI. Additional analyses were performed correcting not only for baseline PASI as a fixed covariate, but for other possible covariates as well. For covariate selection, we performed univariate linear regression analysis for a variety of baseline and treatment characteristics (Table S2). Variables with a *P*-value below 0.05 in univariate analysis were considered for further testing. We then tested these variants for their independent association with ΔPASI using a backward stepwise regression model. Variables that remained independently associated with clinical response in this multivariate model were considered relevant covariates and thus corrected for in the additional analyses. As a supplementary analysis, we also tested for association between genetic variants and achievement of PASI75 and PASI90 after 12 and 24 weeks using binary logistic regression models.

All tests were performed under assumption of an additive genetic model. A Bonferroni-adjusted *P*-value cut-off was used to correct for the total number of genetic variants tested. Analyses were performed in PLINK version 1.9.[20]

Results

Baseline demographics

We included 134 patients treated with either secukinumab or ixekizumab from four European university hospitals (Table 1). The majority of patients were treated with secukinumab (88%). Mean age at start of anti-IL-17A therapy was 44.7 years (SD 13.9) and 92 patients were male (69%). Median baseline PASI was 11.4 (range 2.1–56.7). Mean BMI was 28.6 kg/m^2 (SD 5.3). Twenty-nine patients (22%) had a confirmed diagnosis of psoriatic arthritis. Sixty patients (45%) were naive for biologics at start of anti-IL-17A therapy. Comparison of baseline demographics across the four centres showed differences with respect to baseline PASI (higher in Italy and Estonia), prevalence of psoriatic arthritis (higher in the Netherlands and Italy) and with respect to previous treatments received (higher number of prior conventional systemics and prior biologics in the Netherlands).

Genotyping results

Sequencing of the *IL-17A* exons in the present cohort led to the identification of eight known genetic variants: rs2275913, rs8193037, rs3819025, rs7747909, rs181990814, rs551634550, rs1974226 and rs3748067. None of the identified variants were in the protein-coding region (Table 2). A known or suspected functional effect on *IL-17A* gene expression was described for rs2275913,[12–16] rs8193037,[21] rs3819025,[22] rs7747909,[23]

Table 1 Baseline demographics

	Netherlands (*n* = 45)	Belgium (*n* = 31)	Italy (*n* = 48)	Estonia (*n* = 10)	Full cohort (*n* = 134)
Sex (male), *n* (%)	27 (60)	21 (68)	36 (75)	8 (80)	92 (69)
Ethnicity (Caucasian), *n* (%)	38 (84)	31 (100)	48 (100)	10 (100)	127 (95)
Age at start of anti-IL-17A therapy, years, mean ± SD	45.0 ± 13.6	49.0 ± 14.2	42.3 ± 13.9	41.5 ± 12.4	44.7 ± 13.9
Age at onset of psoriasis, years, median [range]	18 [5–58]	26 [3–70]	21.5 [3–62]	20.5 [13–37]	22 [3–70]
Disease duration, years, median [range]	20 [2–45]	19 [3–47]	16 [0–55]	22.5 [4–31]	18 [0–55]
Psoriatic arthritis† (yes), *n* (%)†	18 (40)	4 (13)	3 (6)	4 (40)	29 (22)
Weight, kg, mean ± SD	94.3 ± 18.9	83.8 ± 14.0	80.9 ± 14.9	92.7 ± 23.2	86.8 ± 17.7
BMI, kg/m^2, mean ± SD	30.4 ± 5.9	28.1 ± 4.7	27.2 ± 5.0	28.7 ± 4.8	28.6 ± 5.3
Baseline PASI, median [range]	9.4 [2.1–40.7]	11.9 [3.0–36.2]	14.7 [8.0–56.7]	21.1 [10.9–36.6]	11.4 [2.1–56.7]
Baseline PASI, mean ± SD	9.8 ± 6.5	12.7 ± 5.9	20.3 ± 12.8	23.0 ± 8.9	15.2 ± 10.5
Prior biological use (yes), *n* (%)	43 (96)	12 (39)	13 (27)	6 (60)	74 (55)
Biologics before anti-IL-17A therapy, *n*, median [range]	3 [0–7]	0 [0–3]	0 [0–5]	1 [0–1]	1 [0–7]
0 prior biologics, *n* (%)	2 (4)	19 (61)	35 (73)	4 (40)	60 (45)
1 prior biologics, *n* (%)	11 (24)	5 (16)	3 (6)	6 (60)	25 (19)
2 prior biologics, *n* (%)	3 (7)	5 (16)	7 (15)	–	15 (11)
3 prior biologics, *n* (%)	13 (31)	2 (7)	1 (2)	–	17 (13)
4 prior biologics, *n* (%)	12 (27)	–	1 (2)	–	13 (10)
≥5 prior biologics, *n* (%)	3 (7)	–	1 (2)	–	4 (3)
Prior conventional/other systemics use (yes), *n* (%)	44 (98)	31 (100)	44 (92)	10 (100)	129 (96)
Conventional/other systemics‡ before anti-IL-17 therapy, *n*, median [range]	3 [0–4]	2 [1–4]	1 [0–3]	2 [1–3]	2 [0–4]

†Percentage based on patients with a diagnosis of psoriatic arthritis as confirmed by a rheumatologist.
‡Conventional and 'other' systemics registered included the following: methotrexate, cyclosporine, retinoids (acitretin or etretinate), fumaric acid esters and apremilast.

rs3748067,[12] and these variants were therefore selected for further analysis (Table 2). All selected genetic variants were in Hardy–Weinberg equilibrium.

Response results

PASI follow-up scores were available for 133 patients at week 12 (primary outcome) and for 109 patients at week 24 (secondary outcome). Reasons for missing values at week 24 were as follows: measurement not done (n = 12), limited follow-up period (n = 8), treatment discontinued within 24 weeks due to side-effects (n = 4) or due to inefficacy (n = 1). Median ΔPASI was −9.8 [range −53.5 to 2.7] at week 12 and −10.0 [range −54.1 to 3.8] at week 24. Median absolute PASI values were 2.3 [range 0 to 30.0] at week 12 and 0.8 [range 0 to 50.5] at week 24. PASI75, PASI90 and PASI100 were achieved in respectively 62%, 39% and 18% of patients after 12 weeks and in 72%, 62% and 28% after 24 weeks. PASI75, PASI90 and PASI100 response rates per SNP genotype are shown in Table S3.

Pharmacogenetic analyses

Influence of genetic variants on ΔPASI at week 12 and 24 In the primary analyses, we tested for association between genetic variants and ΔPASI (corrected for baseline PASI) at week 12. None of the five investigated genetic variants were associated with anti-IL-17A response after 12 weeks (Table 3). For additional covariate correction, we selected prior biological use (biological naivety) and body mass index (BMI) as relevant covariates, based on statistical approaches described previously (Table S2). Biological naivety and a lower body mass index have also shown to be associated with higher effectiveness of biologicals in previous daily practice studies.[24–27] Additional covariate correction for biological naivety and BMI did not change the outcomes of our analyses (Table S4). For the 24 weeks outcome, no associations between genetic variants and ΔPASI were found either (Table 3, Table S4).

Influence of genetic variants on PASI75 and PASI90 response at weeks 12 and 24 Using binary logistic regression, we tested the influence of genetic variants on achievement of PASI75 and PASI90 after 12 and 24 weeks, again with covariate corrections. No significant associations were discovered (Tables S5 and S6).

Discussion

We investigated pharmacogenetics of anti-IL-17A treatment in patients with psoriasis, using a candidate gene approach focused on the protein-coding region of the *IL-17A* gene and surrounding regions important for *IL-17A* expression. A sequencing

Table 2 Identified genetic variants in *IL-17A* gene

Genetic variant	Genomic position†	*IL-17A* position	Nucleotide variant	MAF	Genotypes (*n*)	Functional relevance of minor allele	Selected for analyses
rs2275913	g.52186235	5' UTR	G>A	0.3534	GG/GA/AA : 58/56/19‡	• Increased IL-17 production in AMD[12]/HC[12,13]; increased IL-17 serum levels in VM[14]; decreased IL-17 serum levels in chronic HBV infection/HC[15] and in IS[16]	Yes
rs8193037	g.52186311	5' UTR	G>A	0.0187	GG/GA/AA : 129/5/0	• Increased IL-17 production in NSCLC/HC[21]	Yes
rs3819025	g.52186476	Intron	G>A	0.0709	GG/GA/AA : 116/17/1	• Decreased IL-17 serum levels in BC/HC[22]	Yes
rs7747909	g.52189451	3' UTR	G>A	0.2276	GG/GA/AA : 79/49/6	• Decreased microRNA binding, leading to increased IL-17 production in AMD[23]	Yes
rs181990814	g.52189958	3' UTR	C>A	0.0037	CC/CA/AA : 133/1/0	• Not described/unknown	No
rs551634550	g.52190171	3' UTR	G>A	0.0037	GG/GA/AA : 133/1/0	• Not described/unknown	No
rs1974226	g.52190537	3' UTR	C>T	0.1604	CC/CT/TT : 92/41/1	• Not described/unknown	No
rs3748067	g.52190541	3' UTR	C>T	0.1082	CC/CT/TT : 108/23/3	• Increased IL-17 production in AMD[12]	Yes

†Based on reference sequence built *GRCh38.p12*.
‡One missing genotype for this genetic variant.
AMD, age-related macular degeneration; BC, breast cancer; HBV, hepatitis B virus; HC, healthy controls; IS, ischaemic stroke; MAF, minor allele frequency (in this cohort); NSCLC, non-small-cell lung cancer; UTR, untranslated region.

approach was chosen to allow for potential rare variants to be detected as well. In this multicentre, European cohort of psoriasis patients treated with secukinumab or ixekizumab in daily practice, we were unable to detect genetic variants in the protein-coding region of the *IL-17A* gene. Five common variants in the non-coding DNA of *IL-17A* with possible functional effects were identified, but showed no association with response to IL-17A inhibitors.

Our main finding is that we did not find any variants, common or rare, in the protein-coding region of *IL-17A* in our cohort of 134 psoriasis patients. However, sequencing did identify variants in the periphery of the coding DNA, present in untranslated regions or introns. Out of all variants identified in these regions, we selected only those with a suspected functional effect based on previous research: rs2275913, rs8193037, rs3819025, rs7747909 and rs3748067 (Table 2). The five selected variants were tested for association with clinical response to IL-17A inhibitors secukinumab and ixekizumab after 12 and 24 weeks, using different outcome measures for clinical response (ΔPASI, PASI75, PASI90) with correction for relevant covariates. We found no associations between the genetic variants and response to anti-IL-17A therapy (Table 3, Tables S4–S6).

This is one of the first explorations of pharmacogenetics of the IL-17-class biologicals in psoriasis. Costanzo *et al.*[9] evaluated the influence of *HLA-C*06:02* status on efficacy and safety of secukinumab in a phase III clinical trial of patients with moderate-to-severe psoriasis (SUPREME study). They observed no differences in PASI90 response after 16 weeks of treatment between *HLA-C*06:02* positive and negative patients.[9] Similarly, in a small psoriasis cohort treated with secukinumab in daily practice, Anzengruber *et al.* found that PASI improvement after 12 weeks did not differ between *HLA-C*06:02* positive and

Table 3 Linear regression analyses for association between *IL-17A* polymorphisms and ΔPASI after 12 and 24 weeks of anti-IL-17 treatment, corrected for baseline PASI

Genetic variant	*n*	Allele	Beta	95% CI	*P*-value
Week 12					
rs2275913	132	A	−0.2659	−1.119, 0.5873	0.5424
		G	Ref		
rs8193037	133	A	1.292	−1.829, 4.414	0.4186
		G	Ref		
rs3819025	133	A	−0.03737	−1.632, 1.557	0.9634
		G	Ref		
rs7747909	133	A	0.2668	−0.7545, 1.288	0.6095
		G	Ref		
rs3748067	133	T	0.1327	−1.149, 1.414	0.8395
		C	Ref		
Week 24					
rs2275913	109	A	0.008133	−1.459, 1.475	0.9914
		G	Ref		
rs8193037	109	A	0.8671	−5.41, 7.145	0.7871
		G	Ref		
rs3819025	109	A	−0.2242	−3.035, 2.587	0.8761
		G	Ref		
rs7747909	109	A	1.072	−0.6787, 2.822	0.2328
		G	Ref		
rs3748067	109	T	−1.252	−3.38, 0.8752	0.2512
		C	Ref		

negative patients.[10] To our knowledge, we are the first to systematically investigate pharmacogenetics of the *IL-17A* gene in a large, multicentre daily practice cohort of psoriasis patients treated with secukinumab and ixekizumab.

The present study has several strengths, as well as limitations. This is one the first explorations of pharmacogenetics of IL-17A inhibitors in patients with psoriasis. Using a sequencing approach allowed us to look at the complete coding region of *IL-17A*, rather than focusing solely on common variants using a SNP-based approach. Potential rare variants, for example rare variants in *IL-17A* that are specifically present in the psoriasis population, could have been detected this way as well. Our main limitation is a small cohort size, reducing the chance of finding very rare genetic variants and reducing the power to detect small genetic effects on treatment response. However, very rare variants and very small genetic effects may also be less of interest for the clinical setting, because of their limited usefulness in patient care.

In general, pharmacogenetic studies of biological treatment in psoriasis have thus far generated conflicting and inconclusive results,[5] with the exception of *HLA-C*06:02* which showed to be associated with response to ustekinumab in multiple large cohorts[28–30] and on a meta-analytic level.[31] In rheumatoid arthritis (RA), response to anti-TNF agents is estimated to be explained by genetic factors for 18–87%, depending on outcome definitions and analytic methods used.[32,33] Regardless, genome-wide association studies (GWAS) in RA patients have not uncovered SNPs associated with anti-TNF response on a genomewide significance level.[34–38] This might indicate that heritability of response to biologicals in RA is highly polygenic, with large numbers of variants involved in the outcome, each contributing a small effect.[33] For psoriasis, estimations of heritability of biological response are not available, and large GWAS data are lacking. However, underlying genetic structures regarding response to these drugs in psoriasis patients might very well resemble those in RA. Detecting numerous genetic loci with small genetic effects will require extensive sample sizes, indicating that international consortia will be indispensable in resolving pharmacogenetics of biological treatment.

In summary, we found that the protein-coding region of the *IL-17A* gene is invariable, with no genetic variants discovered in this region amongst 134 patients with psoriasis. A selection of five variants from non-coding regions was evaluated with regards to anti-IL-17A treatment response, but no associations were found. Based on these findings, we conclude that variability in response to IL-17A inhibitors cannot be explained by variation in the protein-coding and untranslated regions of the *IL-17A* gene. Pharmacogenetics of IL-17A inhibitors in the treatment of patients with psoriasis remains to be elucidated, which may be dependent on large scale, non-hypothesis driven genetic association studies.

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Data availability statement

L.J. van Vugt had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Table S1. Primers for IL17A gene
Table S2. Stepwise covariate selection
Table S3. PASI75, PASI90 and PASI100 response rates per SNP-genotype
Table S4. Linear regression analyses for association between *IL17A* polymorphisms and ΔPASI after 12 and 24 weeks of anti-IL17 treatment, corrected for baseline PASI, biological naivety and body mass index
Table S5. Linear regression analyses for association between *IL17A* polymorphisms and ΔPASI after 12 and 24 weeks of anti-IL17 treatment, corrected for baseline PASI, biological naivety and body mass index
Table S6. Binary logistic regression analyses for association between *IL17A* polymorphisms and achievement of PASI75 and PASI90 after 12 and 24 weeks of anti-IL17 treatment, corrected for baseline PASI, biological naivety and body mass index