

Correspondence

The effect of anti-IL-17 treatment on the reaction to a nickel patch test in patients with allergic contact dermatitis

In studies with mice and in nickel-allergic humans, IL-17+ cells have been found in positive patch test reactions indicating that IL-17 may play a crucial role in allergic contact dermatitis (ACD).¹⁻⁴ We conducted a trial (ClinicalTrials.gov, ID: NCT02778711) to examine the effect of anti-IL-17 (secukinumab) in patients with contact allergy.

Patients with a previous ++ or +++ patch test reaction to nickel sulfate were nickel patch tested before (day (D)0) and 1 week after (D14) administration of 300 mg secukinumab (D7). Nickel patch test and skinfold thickness was evaluated on D2/D3/D7 before treatment and on D16/D17/D21 after treatment (unblinded). The clinical reaction was graded using the International Contact Dermatitis Research (ICDRG) scoring system.⁵ Skinfold thickness was measured with a micrometer (Mitutoyo, Tokyo, Japan) as the mean of three measurements (unblinded). Biopsies were taken on D3/D17, stained with hematoxylin and eosin (HE), and analyses for IL-17 were performed using polyclonal antibodies to IL-17 (ab79056; Abcam) (blinded readings).

Eight women and two men completed the study (100%), mean age 48.9 years (range 19–78). All reacted in the patch test; seven had a ++ reaction and three had a +++ reaction. On

D16/D17, 4/10 and 5/10 responded with a slight reduced reaction to nickel compared to before treatment (Table 1). When comparing the overall Wilcoxon signed-rank test results for D2/D16, there was no significant change in response, but when we compared D3/D17, there was a significant reduction in clinical response ($P = 0.034$). For skinfold thickness, mean values ($\pm$ SD) in millimeters were 0.23 ± 0.43 for D2/ 1.21 ± 1.47 for D16, and 0.96 ± 1.46 for D3/ 1.94 ± 1.71 for D17. Thus, an almost significant increase in skinfold thickness compared with D2 was found at D16 ($P = 0.050$), but when comparing D17/D3, no significant increase was seen ($P = 0.103$) (Table 1). There were no detectable differences in inflammation grade in HE-stained biopsies obtained before and after treatment. Quantification of IL-17-positive cells in immunohistochemically stained sections from biopsies was not possible because of weak nuclear staining (Fig. 1).

Administration of secukinumab before patch testing with nickel led to a slight reduced clinical reaction at D17 but not at D16. This finding was not supported by the results of skinfold thickness or histological scoring.

Bechara *et al.*⁶ found that exposure to nickel in human monocyte-derived dendritic cells leads to an upregulation of IL-23, and this cytokine has an important role in the development of Th17 cells and the production of IL-17A, which is in line with

Table 1 Results of patch test scoring and grade of inflammation in skin biopsies before and after administration of secukinumab

Patient no.	Reaction in nickel patch test before secukinumab treatment			Reaction in nickel patch test after secukinumab treatment			Grade of inflammation before secukinumab treatment	Grade of inflammation after secukinumab treatment
	Day 2	Day 3	Day 7	Day 16	Day 17	Day 21	Day 3	Day 17
1	+	++	+? (Reference 5)	++	++	–	2	3
2	+	++	+	+?	+	+	3	3
3	+++	+++	+++	+++	+++	+++	5	4
4	++	+++	+	++	++	+	3	3
5	++	++	+?	+?	++	+?	4	3
6	+	++	+?	+	+?	missing	1	1
7	++	++	+	++	++	+	3	4
8	+++	++	+	++	++	+?	3	3
9	+	++	+	+	+	–	1	2
10	+	++	–	+?	+	–	1	1

For results of patch test scoring on the reaction to nickel, the clinical rating is presented according to the International Contact Dermatitis Research (ICDRG) scoring system. For day 17 versus day 3, $P = 0.03$. All subjects reacted to nickel, and none reacted to the vehicle.

For skin biopsies, the inflammatory score grades were converted to numerical scores, range 1–5 (mild = 1, mild-to-moderate = 2, moderate = 3, moderate-to-severe = 4, and severe = 5). For day 17 versus day 3, no significance was found ($P = 0.67$).

?± Refers to doubtful reaction; faint erythema only.

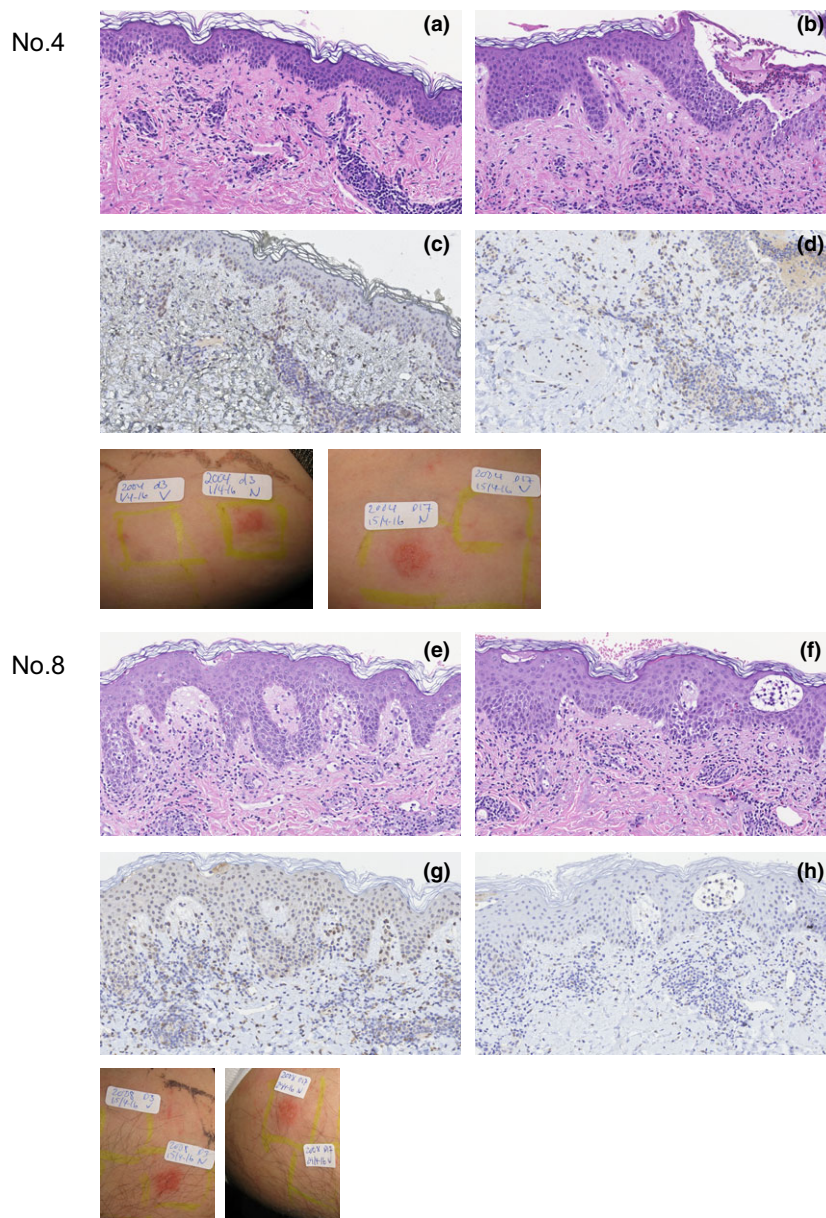


Figure 1 Photographs and histology micrographs from two participants. Skin biopsies were taken from nickel patch test lesions before and after secukinumab treatment: on day 3 (left) and on day 17 (right).

Participant no. 4: hematoxylin and eosin staining, $\times 20$; (a) day 3, moderate inflammation with eosinophils and mild spongiosis; (b) day 17, moderate inflammation with spongiosis and eosinophils; immunohistochemical staining of IL-17, $\times 20$; (c) day 3; (d) day 17.

Participant no. 8: hematoxylin and eosin staining, $\times 20$; (e) day 3, moderate inflammation with eosinophils; (f) day 17, moderate inflammation with spongiosis and eosinophils; immunohistochemical staining of IL-17, $\times 20$, (g) day 3; (h) day 17

the results of a previous study.⁷ However, in another trial we have found minor or no effect of secukinumab in patients with ACD.⁸ Recently, more downstream molecules than IL-17 have been proposed to be a possible target in ACD.⁹

Compared to baseline (D3), five of 10 participants responded at D17 with a slight reduced reaction to nickel after being

treated with secukinumab, which might suggest that secukinumab would have an effect in experimentally-induced ACD. However, at D16 only four of the 10 participants had a reduced reaction to nickel compared to baseline (D2). Treatment with secukinumab did not result in any decrease in skinfold thickness or in the degree of histological inflammation.

Limitations of this study include: (1) only 10 patients were enrolled in the study, (2) readings occurred partly unblinded, and (3) patients were treated with a single dose of secukinumab.

In summary, our data indicate that secukinumab may result in a slight decrease of the clinical scoring of nickel patch test reaction but not in skinfold thickness or inflammation, indicating that anti-IL-17 is not a new potential treatment of ACD.

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