dependent manner. Subsequently, the mean IL-17RA occupancy appeared to decrease with decreasing serum brodalumab concentration (Fig. 2a and b). These results suggested that IL-17RA occupancy correlated with the serum brodalumab concentration.

Brodalumab was well tolerated at a dose from 70 mg to 420 mg SC and 210 mg IV in healthy volunteers and in psoriasis patients (Supplementary Tables S3 and S4 online). Safety profiles were similar for brodalumab and placebo. No deaths, serious adverse events (SAEs), dose-limiting toxicities, or withdrawals due to adverse events (AEs) were reported throughout this study. AEs were all mild or moderate in severity and injection site erythema was the most frequent observation following both placebo and brodalumab administration. No anti-brodalumab antibodies were detected during the study (to Day 64) in any healthy volunteers or psoriasis patients who received brodalumab.

The administration of a single dose of 140 mg or 350 mg SC brodalumab to psoriasis patients resulted in a rapid, dose-dependent improvement in their psoriasis symptoms. The PK and IL-17RA occupancy profiles indicated that IL-17 occupancy remained at the maximum level when the serum brodalumab concentration was more than approximately 1 μg/mL. The serum brodalumab concentration 2 weeks after dosing 140 mg showed more than approximately 1 μg/mL. These findings implied that an interval of approximately 2 weeks between SC brodalumab administration would be reasonable to maintain maximal IL-17RA occupancy. The results of the present study relating to brodalumab safety, PK, PD, and efficacy were highly similar to those obtained in previous studies [8,9]. This indicated that brodalumab has the potential to offer a novel and effective treatment for psoriasis, with a low likelihood of ethnic differences in clinical response. A phase II study of brodalumab in Japanese patients with psoriasis has been recently completed.

Conflict of interest

The authors are the investigators of this study, and have no conflict of interest to declare.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jdermsci.2014.05.007.

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Nemoto Osamu*
Kojinkai Sapporo Skin Clinic, H&B plaza building 5F, S3 w2, Chuo-ku, Sapporo Hokkaido, 060-0063, Japan

Nagashima Hirotaka
Yanagibashi-Clinical Trial Center, Yanagibashi Hospital, Tokyo, Japan

Sayama Koji
Department of Dermatology, Ehime University Graduate School of Medicine, Ehime, Japan

Takazawa Kenji
Shinanozaka Clinic, Medical Corporation Shinanokai, Tokyo, Japan

* Corresponding author. Tel.: +81 11 221 8807;
fax: +81 11 221 5506.
E-mail addresses: osamu.nemo@gmail.com (N. Osamu)
nagashima@y-ctc.com (N. Hirotaka)
sayama@m.ehime-u.ac.jp (S. Koji)
k-takazawa@shinanozaka-clinic.jp (T. Kenji).

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Letter to the Editor

Serum thymus and activation-regulated chemokine (TARC) and interleukin-31 levels as biomarkers for monitoring in adult atopic dermatitis

Dear Editor,

Pruritus is the most vexing problem for patients with atopic dermatitis (AD), but the exact mediator inducing this symptom remains uncertain. Recently, the novel cytokine interleukin-31 (IL-31) has been implicated in the itching associated with AD [1]. We assessed the correlation between well-known various medical mediators such as thymus and activation-regulated chemokine (TARC) and IL-31 levels in serum on the pathogenesis of AD and the disease severity in adult patients with AD. Through this investigation and based on the robust knowledge of AD pathophysiology, we investigated and explored the medical mediators in adult AD patients.

All our patients were enrolled at the St. Marianna University Hospital Department of Dermatology between December 2011 and November 2013. A diagnosis of AD was made according to the clinical and morphological criteria defined by Hanifin and Rajka [2]. Before enrollment, patients did not receive any treatment such as symptomatic therapy (systemic and topical corticosteroids,

immunosuppressive therapy, and anti-histamines) for at least 2 weeks. Only topical emollients were used. Exclusion of other dermatological illnesses was ensured. A total of 12 patients with AD (8 men, 4 women; mean age 33.1 ± 14.1 years) participated in the study.

All adult AD patients were treated with topical corticosteroids in combination with oral antihistamines for 2 weeks during the study. Topical corticosteroids Group 2 (high potency) to Group 4 (medium potency) were used twice daily (morning and evening). All AD patients were also treated with minimal sedation H1 antihistamines (second-generation antihistamines; olopatadine tablets 10 mg or fexofenadine tablets 120 mg). At enrollment and 2 weeks later, all patients were clinically evaluated for Severity index and Pruritus Score. The Severity index was assessed using the SCORAD (Severity SCORing of AD) index, which is commonly used to determine the severity of the disease [3]. The Pruritus Score, as an indication of severity of pruritus, was assessed by a Visual Analogue Scale (VAS) score (0–100) (0: no pruritus, 100: extremely severe pruritus). The SCORAD index and Pruritus Score were assessed as an AD clinical activity index by a dermatologist at 2 weeks compared with baseline data.

Baseline peripheral blood eosinophil count, serum LDH, TARC, tryptase, and IL-31 levels in the AD patients were all significantly higher than those of healthy controls. Clinical improvement was noticeable within 2 weeks of combination therapy using topical corticosteroids and oral antihistamine. Both SCORAD index and Pruritus Score improved significantly after the combination therapy (Fig. 1A and B). No serious systemic adverse events were noted. Peripheral blood eosinophil count, serum LDH, TARC, tryptase levels were significantly decreased by the treatment compared to baseline values (Fig. 1C–F, respectively). Mean serum IL-31 level was lower after treatment compared to baseline, but not significantly (Fig. 1G).

There were significant positive correlations between serum TARC levels and each of SCORAD index and Pruritus Score, indicating TARC levels decrease in concert with decreased severity. There was no significant difference in the other mediators, SCORAD index, or Pruritus Score among our AD patients. There were significant positive correlations between serum TARC levels and each of peripheral blood eosinophil count and serum LDH levels (Fig. 2A and B). We found a significant positive correlation between serum tryptase and peripheral blood eosinophil count (Fig. 2C). Similarly, there was a significant positive correlation between IL-31 levels and LDH levels in serum (Fig. 2D). There was no significant difference among the other mediators in our AD patients.

Topical corticosteroid treatment has been a mainstay in AD therapy and has generally been well tolerated. In addition, antihistamines have been a standard therapy in AD and recommended in many clinical treatment protocols. Our previous study showed the efficacy of antihistamines in relieving pruritus due to AD [4]. Using a combination therapy of topical corticosteroids and oral antihistamine, serum TARC and tryptase levels in adult patients with AD were significantly lower after effective therapy in the present study.

Serum TARC level is regarded as an objective indicator that reflects changes in the skin condition of patients with AD more accurately and sensitively than conventional laboratory measures [5]. The present study demonstrated that serum TARC concentration significantly decreased after effective treatment in parallel with the improvement of clinical symptoms, SCORAD index and Pruritus Score in AD patients. In contrast, we did not find any correlation among other serum biomarkers and SCOARD and VAS scores. Moreover, we found that serum concentration of TARC correlated positively with the number of peripheral blood eosinophils and serum LDH concentration. TARC is a specific chemoattractant for type 2 helper T (Th2) cell

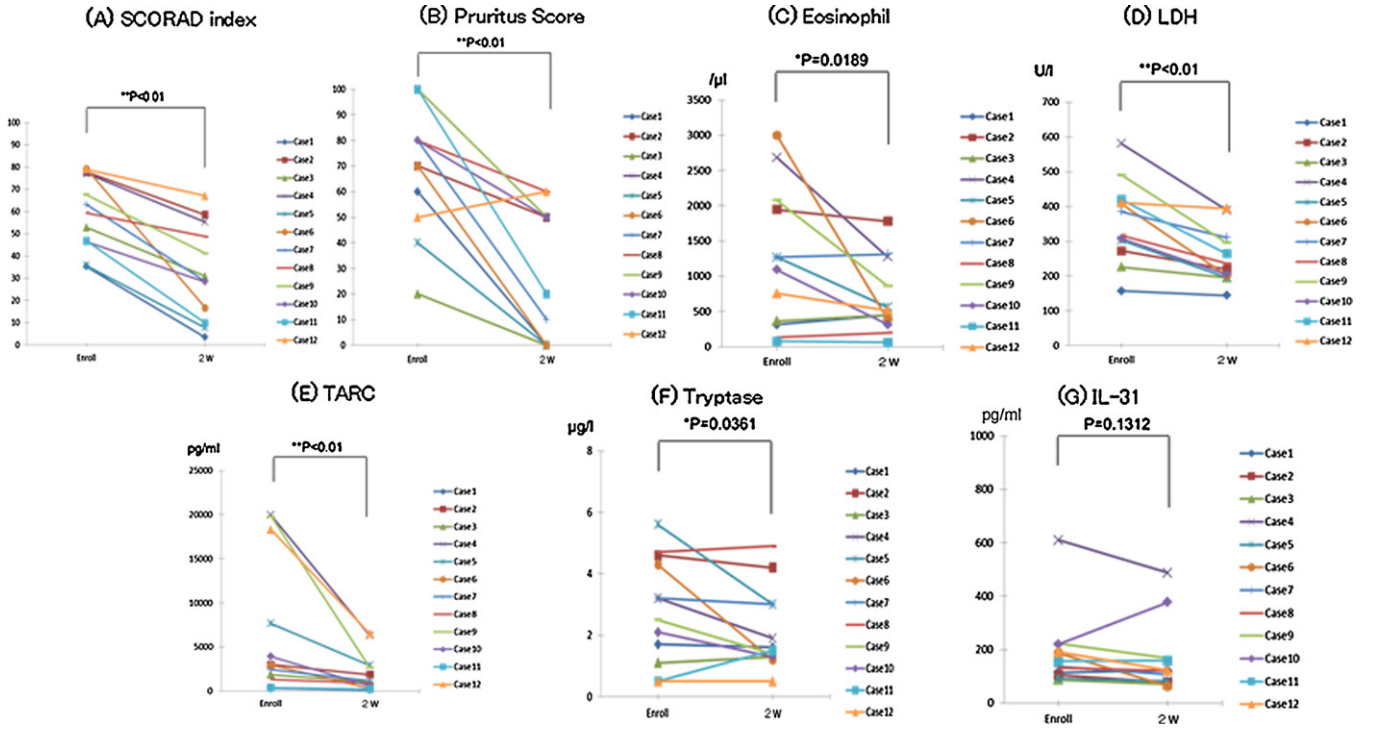

Fig. 1. Efficacy of combination therapy using topical corticosteroids and oral antihistamine in AD – clinical and serological findings. Both SCORAD index and Pruritus Score improved significantly after 2 weeks (A and B). Peripheral blood eosinophil count, serum LDH, TARC, tryptase levels significantly decreased with treatment compared to baseline levels (C–F, respectively). Mean serum IL-31 levels were lower after treatment compared to baseline levels, but not significantly (G).