

LETTER TO THE EDITOR

Reduction of serum thymus and activation-regulated chemokine after short-term intensive therapy may predict better prognosis of moderate to severe atopic dermatitis

Dear Editor,

The goal of treatment for atopic dermatitis (AD) is a state in which symptoms are absent or mild without causing a disturbance to daily life.¹ The Japanese guidelines for the management of AD recommend that dermatitis should be reduced promptly by the remission-induction therapy followed by switching to remission-maintenance therapy.¹ However, there is no evidence that such a prompt improvement of symptoms actually leads to long-lasting, better control of AD than gradual improvement over a long time frame. Serum thymus and activation-regulated chemokine (TARC) closely reflects disease activities of AD.^{2–4} The serum level of 700 pg/mL is often set as a threshold of mild severity of AD.⁵ In order to verify

whether or not prompt improvement is related to long-term remission of AD, we retrospectively examined changes of serum TARC levels, and evaluated whether the short-term (~1 month) effect of remission-induction therapy correlated with the severity of AD 1 year after the intensive inductive treatment.

All clinical records of 446 new AD patients who visited the Department of Dermatology, Hiroshima University Hospital, from July 2013 to December 2017 were reviewed retrospectively. It included 302 adult patients, 50 of whom were examined for serum TARC levels at their first visit, then after an initial short period (1–3 months) and finally after a longer period (8–24 months). They had started intensive therapy to obtain a

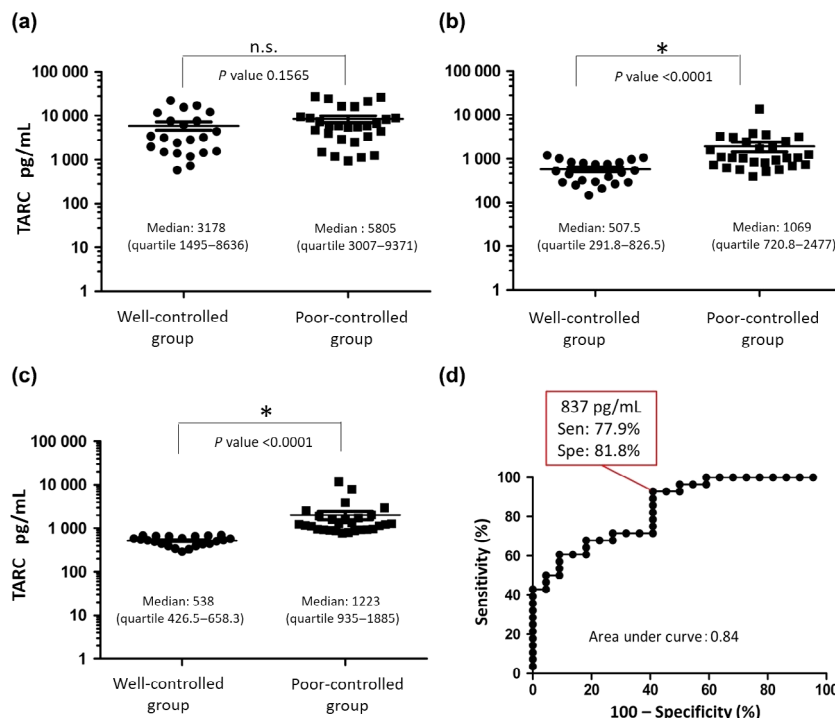


Figure 1. Analysis of thymus and activation-regulated chemokine (TARC) level changes. (a–c) Serum levels of TARC (a) at the first visit, (b) after a short period (1–3 months), (c) after the short period of two groups which was divided based on TARC at a long period (8–24 months) after intensive inductive therapy. Serum levels of TARC at the first visit did not show a statistically significant difference between the groups. However, serum TARC after the short period differed significantly (Mann–Whitney *U*-test, $P < 0.0001$). (d) Receiver–operator curve (ROC) analysis of the short-period TARC levels showed 837 pg/mL as the threshold of the well-controlled group with 75.0% sensitivity and 77.3% specificity. n.s., not significant.

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remission of their symptoms. One year later, 22 of them achieved good control of AD (serum TARC, <700 pg/mL), but the other 28 patients still had high levels of serum TARC (≥ 700 pg/mL). We divided the patients into a well-controlled group and a poor-controlled group based on these long-term TARC levels and retrospectively compared their clinical characteristics (Table S1).

Further analysis revealed that serum levels of TARC at the first visit did not show a statistically significant difference between the groups, although those after the short period differed significantly (Fig 1a–c). Receiver–operator curve analysis of the short-term TARC levels showed 837 pg/mL as the threshold in the well-controlled group (Fig 1d). This result suggests that patients with TARC levels decreasing to 837 pg/mL or less in 1–3 months would achieve long-term, good control of their symptoms.

We cannot deny that patients whose eczema hardly improved might constitutionally have shown high TARC levels over both short and long periods after remission-induction therapy. Nevertheless, the association between long-term AD control and successful reduction of TARC levels in the short term endorses the recommendation in the guideline to promptly reduce symptoms by remission-induction therapy.

This study exhibits the limitations of retrospective small-scale studies. Only patients examined for serum TARC levels were studied, and so might have caused a selection bias. We did not take into account individual patient factors such as seasonal fluctuations or social background. Large-scale and prospective studies are warranted to generate robust evidence to encourage patients with AD to adhere to treatments and inspire confidence in their therapy.

CONFLICT OF INTEREST: None declared.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Clinical characteristics of the well- and poor-controlled groups based on thymus and activation-regulated chemokine (TARC) levels over a long period (8–24 months) after the intensive treatment. The well-controlled group indicates patients who achieved serum TARC levels of less than 700 pg/mL, and the poor-controlled group indicates the patients who still had high levels of serum TARC level (≥ 700 pg/mL). There were no statistically significant differences between the two groups in age, sex, serum total immunoglobulin (Ig)E level or therapies with topical corticosteroids, oral cyclosporin, admission and/or education. Education was aimed at improving patients' understanding of and adherence to appropriate treatments. Age was analyzed by Student's *t*-test, total IgE level by Mann–Whitney *U*-test and the other parameters by the χ^2 -test.

	Well-controlled group (n=22)	Poor-controlled group (n=28)	Statistically significance
Mean Age (year-old)	34.1 (SD 7.3)	32.5 (SD 7.2)	No (P=0.91)
Sex (male/female)	13/9	18/10	No (P=0.71)
Topical corticosteroid	22	27	No (P=0.37)
Oral cyclosporine	2	2	No (P=0.80)
Admission	10	17	No (P=0.28)
Education	21	27	No (P=0.86)
Median total IgE at first visit (IU/mL)	7361 (quartile 3127-15559)	11321 (quartile 3197-16973)	No (P=0.44)