**Supplementary Materials**

**Table S1.** Patient characteristics †

|  |  |  |  |
| --- | --- | --- | --- |
| 　 | Low-dose (20 mL) group (n=19) | High-dose (100 mL) group (n=14) | ‡ p value |
| **Age in years [Median (Range)]**  | 9 (5-12) | 9 (5-15) | 0.706 |
| **Sex (M:F)** | 12:7 | 10:4 | 0.719 |
| **Number of food allergens** | 1 (0-4) | 2 (0-9) | 0.397 |
| **1 (only milk)** | 5 | 2 | 0.397 |
| **2** | 7 | 5 |
| **≥3**  | 7 | 7 |
| **Other allergic disease** |  |  |  |
| **Bronchial asthma** | 12 | 10 | 0.719 |
| **Atopic dermatitis** | 16 | 11 | 1 |
| **Allergic rhinitis** | 10 | 6 | 0.728 |
| **Allergic conjunctivitis** | 6 | 2 | 0.416 |
| **OFC before OIT** |  |  |  |
| **Final dose (mL)** | 1.5 (0.01-10) | 2 (0.1-10) | 0.284 |
| **Laboratory data** |  |  |  |
| **Milk-specific IgE (UA/mL)** | 39.6 (0.41-100) | 28.9 (2.61-84.7) | 0.737 |
| **Casein-specific IgE (UA/mL)** | 45.6 (0.45-100) | 32.0 (16-100) | 0.949 |
| **β-lactoglobulin-specific IgE (UA/mL)** | 1.64 (0.01-57.8) | 2.88 (0.15-63.8) | 0.384 |
| **Milk prick test (mm)** | 10 (6.5-21) | 12.5 (8-18.5) | 0.463 |

OFC, oral food challenge test; OIT, oral immunotherapy

† Data on age, final dose, and laboratory findings are presented as the median and range.

‡ Statistically significant differences were assessed using Mann-Whitney U tests, Fisher’s exact test, or Chi squared (χ2) test. *p* <0.05 was considered statistically significant.

**Table S2.** Age, sex, and the final dose and symptom scores in the open milk challenge tests before and after treatment in the low-dose (20 mL) group

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient**  | **Age** | **Sex** | **Before**  |  | **OIT** | 　 | **After** |
| **No** | **(years)** | Final dose (mL) | Symptom scores † | Maintenance dose at the end of escalation phase (mL) | Maintenance dose end of OIT (mL) | Final dose | Symptom scores † |
| 　 | 　 | (according to Ref 1) |  (mL) | (according to Ref 1) |
| 1 | 9 | F | 5 | G(1)R(2) | 20 | 20 | 20 | S(2)R(3)C(3) |
| 2 | 6 | M | 2 | R(3) | 20 | 20 | 20 | S(2) |
| 3 | 6 | F | 5 | S(1) | 20 | 20 | 100 | 0 |
| 4 | 12 | M | 0.5 | S(1) | 20 | 20 | 10 | S(1)  |
| 5 | 6 | M | 0.5 | S(2)R(2) | 20 | 10 | 50 | S(2) |
| 6 | 9 | F | 0.2 | G(1)  | 5 | 0 | ND | ND |
| 7 | 6 | F | 0.2 | R(3) | 20 | 3 | 10 | 0 |
| 8 | 11 | F | 1 | S(2)G(2)R(2) | 20 | 10 | 5 | R(2) |
| 9 | 6 | F | 0.01 | G(3)  | 20 | 15 | 10 | S(2)G(1) |
| 10 | 10 | M | 10 | S(2)G(2)R(2)C(4) | 20 | 3 | 20 | S(2)G（2）R(3) |
| 11 | 10 | M | 0.5 | G(1)  | 5 | 7 | 20 | S(2) |
| 12 | 11 | M | 2 | R(2)C(3) | 20 | 20 | 5 | S(2)R(3) |
| 13 | 5 | M | 0.5 | R(2) | 20 | 20 | 2 | R(2) |
| 14 | 12 | M | 1 | S(1)G(1) | 20 | 20 | 20 | R(2) |
| 15 | 10 | M | 2 | R(1) | 20 | 20 | 10 | S(2) |
| 16 | 5 | M | 10 | R(3) | 20 | 20 | 5 | R(2) |
| 17 | 7 | F | 2 | S(2)G(1)R(1) | 20 | 20 | 20 | S(2)R(2) |
| 18 | 11 | M | 10 | S(1) | 20 | 20 | 100 | S(1)R(2) |
| 19 | 13 | M | 5 | S(2) | 20 | 20 | 10 | S(2) |

OIT, oral immunotherapy; ND, not done

† Symptom scores indicate the regions of reaction (S, skin symptoms; G, gastrointestinal tract symptoms; R, respiratory tract symptoms; C, cardiovascular symptoms; N, neurological symptoms) and severity grades (1–5) according to the modified Sampson’s anaphylaxis grades in the Japanese Pediatric Guideline for Food Allergy 2012 [1]. The results of the challenge were determined by a doctor. Patient number 7 refused intake of more than 20 ml in the milk challenge test after OIT.

**Table S3.** Age, sex, and the final dose and symptom scores in the open milk challenge tests before and after treatment in the high-dose (100 mL) group

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient**  | **Age** | **Sex** | **Before**  |  | **OIT** | 　 | **After** |
| **No** | **(years)** | Final dose (mL) | Symptom scores † | Maintenance dose at the end of escalation phase (mL) | Maintenance dose at the end of OIT (mL) | Final dose | Symptom scores † |
|  |  | (according to Ref 1) |  (mL) | (according to Ref 1) |
| 1 | 7 | F | 2 | G(2)R(3) | 100 | 100 | 100 | S(1)R(3)  |
| 2 | 6 | M | 1 | S(1)R(3) | 100 | 25 | 5 | S(2) |
| 3 | 7 | M | 10 | S(2) | 100 | 100 | 20 | S(1) |
| 4 | 6 | M | 10 | R(3) | 100 | 100 | 5 | R(2) |
| 5 | 12 | M | 0.1 | G(2) | 60 | 10 | 2 | R(4) |
| 6 | 11 | M | 1 | S(2) | 30 | 30 | 100 | S(2)G(2) |
| 7 | 10 | F | 1 | S(2)R(4) | 30 | 10 | 5 | S(2)R(2)  |
| 8 | 9 | M | 1 | S(1) | 100 | 50 | 10 | S(1) |
| 9 | 9 | M | 0.5 | S(1)G(2) | 0 | 0 | ND | ND |
| 10 | 10 | M | 10 | G(1) | 100 | 100 | 20 | S(2) |
| 11 | 15 | F | 10 | S(1) | 100 | 30 | 20 | S(2)R(4)  |
| 12 | 5 | M | 2 | G(1) | 100 | 40 | 100 | R(2) |
| 13 | 13 | M | 10 | S(1)R(3) | 60 | 60 | 10 | G(1)R(2) |
| 14 | 9 | F | 10 | S(1) | 100 | 100 | 100 | 0 |

OIT, oral immunotherapy; ND, not done

† Symptom scores indicated the regions of reaction (S, skin symptoms; G, gastrointestinal tract symptoms; R, respiratory tract symptoms; C, cardiovascular symptoms; N, neurological symptoms) and severity grades (1–5) according to the modified Sampson’s anaphylaxis grades in the Japanese Pediatric Guideline for Food Allergy 2012 [1]. The results of the challenge were determined by a doctor.

**Table S4.** Laboratory data before OIT and after OIT†

|  |  |  |
| --- | --- | --- |
|  | **Low-dose (20 mL) group (n=18)** | **High-dose (100 mL) group (n=13)** |
| Before | After | p‡ | Before | After | p‡ |
| **Milk-specific IgE [UA/mL, (range)]** | 39.6 (0.41-100) | 24.9 (0.44-100) | 0.061 | 28.9 (2.61-84.7) | 18.0 (6.08-100) | 0.002 |
| **Casein-specific IgE [UA/mL, (range)]** | 45.6 (0.45-100) | 23.0 (0.44-100) | 0.001 | 32.0 (16-100) | 23.3 (5.86-100) | 0.005 |
| **β-lactoglobulin-specific IgE [UA/mL, (range)]** | 1.64 (0.01-57.8) | 0.84 (0.01-29.5) | 0.002 | 2.88 (0.15-63.8) | 1.32 (0.44-53.3) | 0.003 |
| **Milk prick test [mm, (range)]** | 10 (6.5-21) | 8.5 (5.5-12) | 0.007 | 12.5 (8-18.5) | 9.5 (6-14.5) | 0.073 |

OIT, oral immunotherapy

† Values are displayed as the median and range.

‡ Statistically significant differences were assessed using Wilcoxon signed-rank tests in each group. *p* <0.05 was considered statistically significant.



Fig. S1. Study Design

OIT, oral immunotherapy