**SUPPLEMENTARY MATERIALS**

**Table S1.** Schedule of assessments.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Screening(-21 to day 0) | V0(day 0) | Follow-up visits1 | Group A V8Group B V2(2 months ±3 days) | Group A V12Group B V6(6 months ±3 days) | Group A V18Group B V12(12 months ±3 days) |
| Patient information and information consent | X |  |  |  |  |  |
| Review of the inclusion and exclusion criteria | X |  |  |  |  |  |
| Demographic data | X |  |  |  |  |  |
| mARIA classification2 | X |  |  |  |  | X |
| Medical history | X |  |  |  |  | X |
| Skin prick test | X |  |  | X | X | X |
| Blood extraction | X |  |  | X | X | X |
| Nasal challenge and acoustic rhinometry | X |  |  | X | X | X |
| ESPRINT questionnaire | X |  |  | X | X | X |
| Randomization |  | X |  |  |  |  |
| Issue of rescue medication |  | X | X | X | X |  |
| Issue of patient diary |  | X | X | X | X |  |
| Review of patient diary |  |  | X | X | X | X |
| Recording of adverse events | X | X | X | X | X | X |
| Recording of concomitant medication | X | X  | X  | X  | X  | X  |
| Evaluation of patient and investigator satisfaction |  |  |  |  |  | X |

1 Patients had to attend the specialist clinic for a follow-up visits at 2, 3, 4, 5, 7, 8, 9, 10 and 11 months with a window period of ±3 days for the visit at 2 months and ±7 days for other follow-up visits.

2 Valero A, Ferrer M, Sastre J, Navarro AM, Monclús L, Martí-Guadaño E, Herdman M, Dávila I, del Cuvillo A, Colás C, Baró E, Antépara I, Alonso J, Mullol J. A new criterion by which to discriminate between patients with moderate allergic rhinitis and patients with severe allergic rhinitis based on the Allergic Rhinitis and its Impact on Asthma severity items. J Allergy Clin Immunol. 2007 Aug;120(2):359-65.

**Table S2.** Allergen1 injected in the induction phase (first 8 weeks of treatment)

|  |  |  |
| --- | --- | --- |
| Week | Vial number2 | ml |
| 1 | 2 | 0.1 |
| 2 | 2 | 0.2 |
| 3 | 2 | 0.4 |
| 4 | 2 | 0.8 |
| 5 | 3 | 0.1 |
| 6 | 3 | 0.2 |
| 7 | 3 | 0.4 |
| 8 | 3 | 0.8 |

1 Allergen extracts were adsorbed onto preformed aluminum hydroxide gel. It was prepared in individual therapeutic solutions, according to the composition specified in the medical prescription.In this study, standardized extracts with a 50:50 mixture of *Dermatophagoides pteronyssinus* and *D. farinae* were used.

2 Vial number 2 contained 1 IR/mL of allergen extract; vial number 3 contained 10 IR/mL of allergen extract. An Index of Reactivity (IR) of 100 RI/ml was assigned to the concentration of extract which, in skin prick tests using Stallerpoint® lancets®, caused a 7 mm (geometric mean) papule in 30 patients sensitized to the allergen in question.

**Table S3.** VAS overall score of AR-related symptoms.

|  |  |  |  |
| --- | --- | --- | --- |
| **Concentration** | **Visit** | **Group A** | **Group B** |
| 0.1  | Baseline | 5.1 (2.38) | 3.4 (2.56) |
| 12 months | 2.1 (1.92) | 2.1 (1.17) |
| 1  | Baseline | 6.5 (2.06) | 4.7 (2.49) |
| 12 months | 3.2 (2.05) | 3.4 (1.51) |
| 10  | Baseline | 8.1 (1.83) | 6.8 (2.28) |
| 12 months | 4.9 (2.60) | 5.7 (2.78) |

All values represent mean (SD)

**Table S4.** Average Rhinitis Total Symptom Score (ARTSS).

|  |  |  |
| --- | --- | --- |
| **Visit** | **Group A** | **Group B** |
| Baseline | 3.5 (2.55) | 3.6 (2.39) |
| 2 months | 1.9 (1.72) | 2.7 (1.72) |
| 6 months | 2.0 (2.12) | 2.6 (2.58) |
| 12 months | 2.1 (2.26) | 3.0 (3.19) |

All values represent mean (SD)

**Table S5.** Rescue Medication Score (ARMS).

|  |  |  |
| --- | --- | --- |
| **Visit** | **Group A** | **Group B** |
| Baseline | 1.1 (0.94) | 1.6 (1.13) |
| 2 months | 0.6 (0.85) | 1.1 (1.07) |
| 6 months | 0.4 (0.62) | 1.0 (0.95) |
| 12 months | 0.5 (0.85) | 1.3 (1.10) |

All values represent mean (SD)

**Table S6.** Average total adjusted Symptom Score (AdSS).

|  |  |  |
| --- | --- | --- |
| **Visit** | **Group A** | **Group B** |
| Baseline | 4.0 (2.86) | 4.1 (2.76) |
| 2 months | 2.1 (1.78) | 3.1 (2.22) |
| 6 months | 2.1 (2.15) | 2.8 (2.84) |
| 12 months | 2.2 (2.26) | 3.2 (3.28) |

All values represent mean (SD)

**Table S7.** AR symptoms (TNSS).

|  |  |  |  |
| --- | --- | --- | --- |
| **Symptom** | **Visit** | **GroupA** | **Group B** |
| Nasal obstruction  | Baseline | 1.2 (0.87) | 0.9 (0.62) |
| 12 months | 0.7 (0.71) | 0.7 (0.83) |
| Sneezing  | Baseline | 0.8 (0.66) | 1.0 (0.75) |
| 12 months | 0.6 (0.67) | 1.0 (0.87) |
| Rhinorrhea  | Baseline | 0.9 (0.71) | 0.9 (0.76) |
| 12 months | 0.5 (0.71) | 0.8 (0.86) |
| Nasal itching  | Baseline | 0.7 (0.71) | 0.8 (0.72) |
| 12 months | 0.4 (0.54) | 0.6 (0.92) |

All values represent mean (SD)

**Table S8.** ESPRINT-15 questionnaire.

|  |  |  |  |
| --- | --- | --- | --- |
| **Domain** | **Visit** | **Group A** | **Group B** |
| Symptoms  | Baseline | 3.0 (1.48) | 2.9 (1.29) |
| 12 months | 1.5 (1.30) | 2.2 (1.54) |
| Daily living  | Baseline | 2.3 (1.70) | 2.0 (1.59) |
| 12 months | 1.1 (1.44) | 2.0 (2.26) |
| Sleep  | Baseline | 2.3 (1.86) | 2.5 (1.59) |
| 12 months | 1.3 (1.63) | 1.8 (1.87) |
| Psychological  | Baseline | 2.8 (1.93) | 2.4 (1.79) |
| 12 months | 1.1 (1.52) | 1.7 (1.80) |
| General health  | Baseline | 3.4 (0.88) | 3.2 (0.98) |
| 12 months | 2.7 (0.81) | 2.8 (1.12) |
| Global  | Baseline | 2.6 (1.55) | 2.5 (1.28) |
| 12 months | 1.3 (1.32) | 1.9 (1.67) |

All values represent mean (SD)

**Table S9.** Skin prick-test. Safety population (N=56)

|  |  |  |  |
| --- | --- | --- | --- |
| **Visit** | **HDM** | **Group A** | **Group B** |
| Baseline | *D. pteronyssinus* | 8.4 (6.5 - 11.0) | 6.9 (5.5 - 8.3) |
| *D. farinae* | 7.8 (5.5 - 9.3) | 6.3 (5.0 - 8.3) |
| 2 months | *D. pteronyssinus* | 6.8 (5.3 - 8.3) | 7.4 (4.9 - 9.6) |
| *D. farinae* | 6.3 (5.0 - 7.8) | 7.5 (6.1 - 9.3) |
| 6 months | *D. pteronyssinus* | 7.0 (5.0 - 9.3) | 7.8 (5.3 - 8.3) |
| *D. farinae* | 6.3 (5.5 - 8.8) | 6.5 (5.3 - 7.5) |
| 12 months | *D. pteronyssinus* | 6.8 (5.8 - 8.8) | 9.3 (6.8 - 12.5) |
| *D. farinae* | 7.0 (5.5 - 9.3) | 7.3 (5.5 - 14.3) |

All values represent median (Q1 - Q3)

**Table S10.** Differences inthe SPT with respect to baseline. Safety population.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Visit** | **Species** |  | **Group A** | **Group B** |
| 2 months | *D. pteronyssinus* | Difference1 | -1.5 (-3.0 - 0.5) | -0.1 (-1.8 - 2.0) |
| p2 | 0.0089 | 0.8356 |
| *D. farinae* | Difference1 | -1.3 (-2.8 - 0.3) | 1.1 (-0.1 - 4.0) |
| p2 | 0.0006 | 0.1392 |
| 6 months | *D. pteronyssinus* | Difference1 | -0.8 (-4.0 - 1.5) | 0.0 (-0.8 - 2.5) |
| p2 | 0.2485 | 0.4863 |
| *D. farinae* | Difference1 | -1.0 (-3.0 - 0.8) | 0.5 (-1.8 - 2.3) |
| p2 | 0.0926 | 0.9451 |
| 12 months | *D. pteronyssinus* | Difference1 | -1.0 (-3.8 - 2.3) | 2.6 (-0.8 - 6.0) |
| p2 | 0.3514 | 0.0776 |
| *D. farinae* | Difference1 | -0.3 (-1.8 - 2.5) | 1.1 (-0.8 - 5.0) |
| p2 | 0.7865 | 0.1779 |

1 median (Q1 - Q3)

2 Wilcoxon test