

## SUPPLEMENTARY MATERIAL

Table 1S. Sociodemographic and clinical characteristics

| Characteristics   | N (300) |        |
|---|---------|--------|
| Age at reference date*  |         |        |
| Median (Q1, Q3)   | 50      | 39; 62 |
|   | N       | %      |
| Sex   |         |        |
| Male  | 83      | 27,7%  |
| Female  | 217     | 72,3%  |
| Working status  |         |        |
| Employed, full-time   | 151     | 50,3%  |
| Employed, part-time   | 30      | 10,0%  |
| Homemaker   | 29      | 9,7%   |
| Student   | 13      | 4,3%   |
| Unemployed  | 16      | 5,3%   |
| Retired   | 45      | 15,0%  |
| Disabled  | 7       | 2,3%   |
| Other   | 9       | 3,0%   |
| Comorbidities <sup>1</sup>  |         |        |
| Do not know/no comorbidities  | 25      | 8,3%   |
| With comorbidities  | 275     | 91,7%  |
| Presence of allergic sensitization (diagnosed by blood or skin testing) | 150     | 50,0%  |
| Allergic rhinitis   | 108     | 36,0%  |
| Heart disease   | 17      | 5,7%   |
| Anxiety   | 77      | 25,7%  |
| Anaphylaxis   | 21      | 7,0%   |
| Arthritis   | 28      | 9,3%   |
| Aspirin sensitivity   | 25      | 8,3%   |
| Atopic dermatitis/Eczema  | 46      | 15,3%  |
| Chronic bronchitis  | 21      | 7,0%   |
| Chronic Obstructive Pulmonary Disease (COPD)                            | 9       | 3,0%   |
| Chronic sinusitis   | 27      | 9,0%   |
| Depression  | 51      | 17,0%  |
| Diabetes  | 17      | 5,7%   |
| Emphysema   | 5       | 1,7%   |
| GERD (heartburn/reflux)   | 64      | 21,3%  |
| Hypertension  | 52      | 17,3%  |
| Chronic rhinosinusitis with Nasal Polyps                                | 42      | 14,0%  |
| Sleep Apnea   | 25      | 8,3%   |
| Stroke  | 3       | 1,0%   |
| Others  | 44      | 14,7%  |
| Clinician-reported  |         |        |

|  |          |          |
|--|----------|----------|
| Age at initial diagnosis (years)   |          |          |
| Median (Q1, Q3)  | 30       | 14; 46   |
| Years since initial diagnosis  |          |          |
| Median (Q1, Q3)  | 13       | 6; 29    |
| Spirometry performed in the last year  |          |          |
| Yes  | 256      | 85,3%    |
| No   | 44       | 14,7%    |
| Asthma medications   |          |          |
| ICS (monotherapy)  | 12       | 4,0%     |
| ICS + LABA   | 243      | 81,0%    |
| LAMA   | 100      | 33,3%    |
| LTRA   | 66       | 22,0%    |
| SABA   | 10       | 3,3%     |
| OCS  | 16       | 5%       |
| Biologics  | 30       | 10%      |
| Exacerbations experienced in the last year   |          |          |
| Number of patients with a severe exacerbation  | 116      | 38,7%    |
| Number of patients with an exacerbation that resulted in hospitalization for asthma for $\geq 24$ hours  | 21       | 7,0%     |
| <b>Number of severe exacerbations</b>  | <b>N</b> | <b>%</b> |
| Mean (SD)  | 0,8      | 1,31     |
| Median (Q1, Q3)  | 0        | 0; 1     |
| Min, max   | 0        | 6        |
| Number of exacerbations requiring short term OCS treatment for at least three days AND/OR increase of OCS dosis <sup>1</sup>                                       |          |          |
| Mean (SD)  | 1,1      | 1,14     |
| Median (Q1, Q3)  | 1        | 0; 1     |
| Min, max   | 0        | 5        |
| Number of exacerbations requiring visit to an emergency room (stay $\geq 24$ hours), unplanned office visit or treatment with systemic corticosteroid <sup>1</sup> |          |          |
| Mean (SD)  | 0,8      | 0,8      |
| Median (Q1, Q3)  | 1        | 0; 1     |
| Min, max   | 0        | 4        |
| Number of exacerbations that resulted in hospitalization for asthma for $\geq 24$ hours  |          |          |
| Mean (SD)  | 0,2      | 0,58     |
| Median (Q1, Q3)  | 0        | 0; 0     |
| Min, max   | 0        | 4        |

\*Out of 300 patients, 2 (0.7%) were adolescents (<18 years old)

Abbreviations: GERD, gastroesophageal reflux disease; ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; SABA, short-acting beta-agonist.

Table 2S. Asthma control definition

| Asthma control levels  | ACT   | Exacerbations  |  | ACQ-6   | AIRQ |
|------------------------|-------|--|--|---------|------|
|                        |       | Use of OCS or emergency visits /no planned in the last 12 months | Hospitalisations in the last 12 months |         |      |
| Well controlled        | ≥20   | 0  | 0                                      | ≤0,7    | ≤1   |
| Not well controlled    | 16-19 | 1  | 0                                      | 0,8-1,5 | 2-4  |
| Very poorly controlled | ≤15   | ≥2   | ≥1                                     | >1,5    | ≥5   |

<sup>1</sup>Among patients suffering any severe exacerbations

Table 3S. Performance characteristics of the AIRQ questionnaire for the Spanish cohort based on the participant's ACT score plus exacerbation history

| AIRQ Models                           | Full Analysis Set (FAS) |      |             |             |                           |                           |         |       |           |
|---------------------------------------|-------------------------|------|-------------|-------------|---------------------------|---------------------------|---------|-------|-----------|
|                                       | LR+                     | LR-  | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value | AIC     | AUC   | Model Fit |
| <b>Univariate Model 1<sup>1</sup></b> |                         |      |             |             |                           |                           |         |       |           |
| <b>AIRQ score cut-off</b>             |                         |      |             |             |                           |                           |         |       |           |
| ≥ 1                                   | 2,37                    | 0,04 | 97.7%       | 58.8%       | 85.7%                     | 90.9%                     | 238,467 | 78.2% |           |
| ≥ 2                                   | 6,33                    | 0,12 | 89.3%       | 85.9%       | 94.1%                     | 76.0%                     | 200,992 | 87.6% |           |
| ≥ 3                                   | 16,01                   | 0,26 | 75.3%       | 95.3%       | 97.6%                     | 60.4%                     | 221,578 | 85.3% |           |
| ≥ 4                                   | 53,37                   | 0,38 | 62.8%       | 98.8%       | 99.3%                     | 51.2%                     | 243,073 | 80.8% |           |
| ≥ 5                                   | 0                       | 0,51 | 48.8%       | 100%        | 100%                      | 43.6%                     | 271,113 | 74.4% | *         |
| ≥ 6                                   | 0                       | 0,62 | 38.1%       | 100%        | 100%                      | 39.0%                     | 295,556 | 69.1% | *         |
| ≥ 7                                   | 0                       | 0,74 | 25.6%       | 100%        | 100%                      | 34.7%                     | 320,31  | 62.8% | *         |
| ≥ 8                                   | 0                       | 0,81 | 19.1%       | 100%        | 100%                      | 32.8%                     | 331,835 | 59.5% | *         |
| ≥ 9                                   | 0                       | 0,92 | 8.4%        | 100%        | 100%                      | 30.1%                     | 349,203 | 54.2% | *         |
| = 10                                  | 0                       | 0,98 | 1.9%        | 100%        | 100%                      | 28.7%                     | 358,958 | 50.9% | *         |
| <b>Univariate Model 2<sup>2</sup></b> |                         |      |             |             |                           |                           |         |       |           |
| <b>AIRQ score cut-off</b>             |                         |      |             |             |                           |                           |         |       |           |
| ≥ 1                                   | 1.44                    | 0    | 100%        | 30.4%       | 48.6%                     | 100%                      | 343,442 | 65.2% | *         |
| ≥ 2                                   | 2,05                    | 0,03 | 98.3%       | 51.9%       | 57.4%                     | 97.9%                     | 301,819 | 75.1% |           |
| ≥ 3                                   | 2,99                    | 0,11 | 92.4%       | 69.1%       | 66.3%                     | 93.3%                     | 282,227 | 80.7% |           |
| ≥ 4                                   | 4,56                    | 0,18 | 85.7%       | 81.2%       | 75.0%                     | 89.6%                     | 266,195 | 83.5% |           |
| ≥ 5                                   | 8,46                    | 0,28 | 74.8%       | 91.2%       | 84.8%                     | 84.6%                     | 261,068 | 83.0% |           |
| ≥ 6                                   | 16,30                   | 0,38 | 63.0%       | 96.1%       | 91.5%                     | 79.8%                     | 271,116 | 79.6% |           |
| ≥ 7                                   | 40,31                   | 0,56 | 44.5%       | 98.9%       | 96.4%                     | 73.1%                     | 306,681 | 71.7% |           |
| ≥ 8                                   | 60,84                   | 0,67 | 33.6%       | 99.4%       | 97.6%                     | 69.5%                     | 332,002 | 66.5% |           |
| ≥ 9                                   | 0                       | 0,85 | 15.1%       | 100%        | 100%                      | 64.2%                     | 371,925 | 57.6% | *         |
| = 10                                  | 0                       | 0,97 | 3.4%        | 100%        | 100%                      | 61.1%                     | 399,502 | 51.7% | *         |

\*Quasi-complete separation of data points. The maximum likelihood estimate does not exist at this point. The validity of the model fit is questionable for this cut-off point

<sup>1</sup>Model 1 compared well-controlled vs. not well-controlled/very poorly controlled asthma

<sup>2</sup>Model 2 compared well-controlled/not well-controlled vs. very poorly controlled asthma

<sup>3</sup>Multivariate-adjusted model for age, sex, and asthma medication

Table 4S. Performance characteristics of the AIRQ questionnaire for the Spanish cohort based on the participant's ACQ-6 score plus exacerbation history

| AIRQ Models                           | Full Analysis Set (FAS) |      |             |             |                           |                           |         |       | Model Fit |
|---------------------------------------|-------------------------|------|-------------|-------------|---------------------------|---------------------------|---------|-------|-----------|
|                                       | LR+                     | LR-  | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value | AIC     | AUC   |           |
| <b>Univariate Model 1<sup>1</sup></b> |                         |      |             |             |                           |                           |         |       |           |
| <b>AIRQ score cut-off</b>             |                         |      |             |             |                           |                           |         |       |           |
| ≥ 1                                   | 2,17                    | 0,04 | 97.6%       | 54.9%       | 83.3%                     | 90.9%                     | 258,821 | 76.3% |           |
| ≥ 2                                   | 4,50                    | 0,14 | 89.0%       | 80.2%       | 91.2%                     | 76.0%                     | 231,477 | 84.6% |           |
| ≥ 3                                   | 8,60                    | 0,27 | 75.6%       | 91.2%       | 95.2%                     | 61.9%                     | 246,176 | 83.4% |           |
| ≥ 4                                   | 14,37                   | 0,39 | 63.2%       | 95.6%       | 97.1%                     | 53.0%                     | 266,834 | 79.4% |           |
| ≥ 5                                   | 22,42                   | 0,52 | 49.3%       | 97.8%       | 98.1%                     | 45.6%                     | 292,648 | 73.5% |           |
| ≥ 6                                   | 35,27                   | 0,62 | 38.8%       | 98.9%       | 98.8%                     | 41.3%                     | 310,356 | 68.8% |           |
| ≥ 7                                   | 23,51                   | 0,75 | 25.8%       | 98.9%       | 98.2%                     | 36.7%                     | 336,185 | 62.4% |           |
| ≥ 8                                   | 17,42                   | 0,82 | 19.1%       | 98.9%       | 97.6%                     | 34.7%                     | 347,968 | 59.0% |           |
| ≥ 9                                   | 0                       | 0,91 | 8.6%        | 100%        | 100%                      | 32.3%                     | 358,691 | 54.3% | *         |
| = 10                                  | 0                       | 0,98 | 1.9%        | 100%        | 100%                      | 30.7%                     | 369,282 | 51.0% | *         |
| <b>Univariate Model 2<sup>2</sup></b> |                         |      |             |             |                           |                           |         |       |           |
| <b>AIRQ score cut-off</b>             |                         |      |             |             |                           |                           |         |       |           |
| ≥ 1                                   | 1,49                    | 0,02 | 99.3%       | 33.3%       | 55.9%                     | 98.2%                     | 350,198 | 66.3% |           |
| ≥ 2                                   | 2,30                    | 0,04 | 97.8%       | 57.4%       | 66.2%                     | 96.9%                     | 291,762 | 77.6% |           |
| ≥ 3                                   | 3,70                    | 0,12 | 91.3%       | 75.3%       | 75.9%                     | 91.0%                     | 268,129 | 83.3% |           |
| ≥ 4                                   | 5,77                    | 0,21 | 81.9%       | 85.8%       | 83.1%                     | 84.8%                     | 267,648 | 83.8% |           |
| ≥ 5                                   | 12,52                   | 0,32 | 69.6%       | 94.4%       | 91.4%                     | 78.5%                     | 268,618 | 82.0% |           |
| ≥ 6                                   | 22,89                   | 0,45 | 56.5%       | 97.5%       | 95.1%                     | 72.5%                     | 292,503 | 77.0% |           |
| ≥ 7                                   | 63,39                   | 0,61 | 39.1%       | 99.4%       | 98.2%                     | 65.7%                     | 329,023 | 69.3% |           |
| ≥ 8                                   | 46,96                   | 0,71 | 29.0%       | 99.4%       | 97.6%                     | 62.2%                     | 356,974 | 64.2% |           |
| ≥ 9                                   | 0                       | 0,87 | 13.0%       | 100%        | 100%                      | 57.4%                     | 388,656 | 56.5% | *         |
| = 10                                  | 0                       | 0,97 | 2.9%        | 100%        | 100%                      | 54.7%                     | 411,691 | 51.4% | *         |

\*Quasi-complete separation of data points. The maximum likelihood estimate does not exist at this point. The validity of the model fit is questionable for this cut-off point

<sup>1</sup>Model 1 compared well-controlled vs. not well-controlled/very poorly controlled asthma

<sup>2</sup>Model 2 compared well-controlled/not well-controlled vs. very poorly controlled asthma

<sup>3</sup>Multivariate-adjusted model for age, sex, and asthma medication

Table 5S. Agreement between AIRQ, ACT, and ACQ-6 score and physician assessment of asthma control

|                              | Full Analysis Set (FAS)                               |       |                 |                     |       |                 |                   |       |                 |                                |                     |
|------------------------------|---|-------|-----------------|---------------------|-------|-----------------|-------------------|-------|-----------------|--------------------------------|---------------------|
|                              | Physician global assessment of patient asthma control |       |                 |                     |       |                 |                   |       |                 |                                |                     |
|                              | Well controlled                                       |       |                 | Not well controlled |       |                 | Poorly controlled |       |                 | Weighted<br>Kappa <sup>1</sup> | 95% CI <sup>2</sup> |
|                              | N   | %     | 95% CI          | N                   | %     | 95% CI          | N                 | %     | 95% CI          |                                |                     |
| <b>AIRQ score assessment</b> | <b>102</b>  |       |                 | <b>124</b>          |       |                 | <b>74</b>         |       |                 |                                |                     |
| Missing                      | 0   | 0%    | 0%; 3.6%        | 0                   | 0%    | 0%; 2.9%        | 0                 | 0%    | 0%; 4.9%        | 0,62                           | 0.55; 0.68          |
| Well controlled              | 77  | 75.5% | 66.0%;<br>83.5% | 18                  | 14.5% | 8.8%;<br>22.0%  | 1                 | 1.4%  | 0.0%; 7.3%      |                                |                     |
| Not well controlled          | 25  | 24.5% | 16.5%;<br>34.0% | 63                  | 50.8% | 41.7%;<br>59.9% | 11                | 14.9% | 7.7%;<br>25.0%  |                                |                     |
| Very poorly controlled       | 0   | 0%    | 0%; 3.6%        | 43                  | 34.7% | 26.4%;<br>43.7% | 62                | 83.8% | 73.4%;<br>91.3% |                                |                     |
| <b>ACT assessment</b>        | <b>102</b>  |       |                 | <b>124</b>          |       |                 | <b>74</b>         |       |                 |                                |                     |
| Missing                      | 0   | 0%    | 0%; 3.6%        | 0                   | 0%    | 0%; 2.9%        | 0                 | 0%    | 0%; 4.9%        | 0,71                           | 0.64; 0.77          |
| Well controlled              | 87  | 85.3% | 76.9%;<br>91.5% | 13                  | 10.5% | 5.7%;<br>17.3%  | 2                 | 2.7%  | 0.3%; 9.4%      |                                |                     |
| Not well controlled          | 15  | 14.7% | 8.5%;<br>23.1%  | 76                  | 61.3% | 52.1%;<br>69.9% | 8                 | 10.8% | 4.8%;<br>20.2%  |                                |                     |
| Very poorly controlled       | 0   | 0%    | 0%; 3.6%        | 35                  | 28.2% | 20.5%;<br>37.0% | 64                | 86.5% | 76.5%;<br>93.3% |                                |                     |
| <b>ACQ-6 assessment</b>      | <b>102</b>  |       |                 | <b>124</b>          |       |                 | <b>74</b>         |       |                 |                                |                     |
| Missing                      | 0   | 0%    | 0%; 3.6%        | 0                   | 0%    | 0%; 2.9%        | 0                 | 0%    | 0%; 4.9%        | 0,59                           | 0.51; 0.65          |
| Well controlled              | 87  | 85.3% | 76.9%;<br>91.5% | 24                  | 19.4% | 12.8%;<br>27.4% | 5                 | 6.8%  | 2.2%;<br>15.1%  |                                |                     |
| Not well controlled          | 12  | 11.8% | 6.2%;<br>19.6%  | 45                  | 36.3% | 27.8%;<br>45.4% | 6                 | 8.1%  | 3.0%;<br>16.8%  |                                |                     |
| Very poorly controlled       | 3   | 2.9%  | 0.6%; 8.4%      | 55                  | 44.4% | 35.4%;<br>53.5% | 63                | 85.1% | 75.0%;<br>92.3% |                                |                     |

<sup>1</sup>Weighted Kappa was calculated using Cicchetti-Allison weights (linear weights)<sup>2</sup>Kappa 1,000 bootstrap sample was used to calculate 95%CI