**Online Supplementary tables and figures**

**Supplementary Table S1: Omalizumab responders vs non-responders**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Omalizumab responder N = 92, 88.5%** | **Omalizumab non-responder  N = 12, 11.5%** |  |
|  | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | **P-value** |
| **Annual rate of exacerbations in the past year, median (IQR)**  | 5 (2) | 1 | 4 (4) | 1 | 0.055 |
| **Annual rate of AHE in the past year, median (IQR)**  | 0 (2) | 8 | 2 (2) | 1 | 0.141 |
| **Maximum IgE in the past year, median (IQR) - kU/L**  | 260.8 (388.6) | 2 | 107 (536.1) | 1 | 0.569 |
| **Maximum PBE count in the past year, median (IQR) -cells/µL**  | 200 (400) | 7 | 250 (775) | 2 | 0.605 |
| **Baseline ACQ6, mean (SD)**  | 2.95 (1.28) | 20 | 2.85 (0.78) | 5 | 0.769 |
| **Baseline FENO, median (IQR) - ppb**  | 29.5 (37) | 24 | 14 (52.21) | 3 | 0.536 |
| **Baseline Maintenance OCS dose, median (IQR) - mg**  | 10 (13) | 1 | 10 (20) | 0 | 0.291 |
| **Baseline Clinic FEV1%, mean (SD)**  | 68.13 (20.49) | 6 | 58.30 (20.22) | 1 | 0.137 |
| **BMI, median (IQR) - kgm-2**  | 30.36 (5.99) | 0 | 36.77 (10.03) | 0 | 0.051 |
| **Age of asthma diagnosis, median (IQR) - y** | 11 (25.50) | 3 | 8 (12) | 1 | 0.323 |
| **Age at study, mean (SD) - y** | 53 (15) | 0 | 44 (12) | 0 | **0.025** |
|  | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **P-value** |
| **Multiple (>1) AHE in the past year, Yes** | 27.4% (23) | 8 | 54.5% (6) | 1 | 0.085 |
| **On Maintenance OCS at baseline, Yes** | 46.7% (43) | 0 | 58.3% (7) | 0 | 0.450 |
| **Adult-onset asthma, Yes**  | 39.3% (35) | 1 | 18.2% (2) | 1 | 0.205 |
| **Sex, Male**  | 35.9% (33) | 0 | 8.3% (1) | 0 | 0.098 |
| **Ethnicity, White**  | 89.1% (82) | 0 | 83.3% (10) | 0 | 0.627 |
| **Rhinitis, Ever**  | 73.0% (54) | 22 | 83.3% (10) | 0 | 0.723 |
| **GORD, Ever**  | 64.1% (59) | 0 | 63.6% (7) | 1 | 1.000 |
| **Smoking history, Ever**  | 43.5% (40) | 0 | 41.7% (5) | 0 | 0.905 |
| **Obesity (BMI≥30kgm-2), Ever**  | 50.0% (46) | 0 | 75.0% (9) | 0 | 0.103 |
| **ICU admission for asthma, Ever**  | 26.4% (24) | 1 | 41.7% (5) | 0 | 0.311 |
| **Intubation for asthma, Ever**  | 14.3% (13) | 1 | 16.7% (2) | 0 | 0.686 |
| **Dysfunctional breathing, Ever**  | 48.8% (42) | 6 | 66.7% (8) | 0 | 0.247 |
| **ILO, Ever**  | 17.5% (14) | 12 | 33.3% (4) | 0 | 0.241 |
| **Depression, Ever**  | 30.4% (24) | 13 | 45.5% (5) | 1 | 0.316 |
| **Anxiety, Ever**  | 26.6% (21) | 13 | 63.6% (7) | 1 | **0.031** |
| **Bronchiectasis, Ever**  | 14.4% (13) | 2 | 16.7% (2) | 0 | 1.000 |
| **Salicylate sensitivity, Ever**  | 33.3% (30) | 2 | 33.3% (4) | 0 | 1.000 |
| **ABPA, Ever**  | 12.2% (11) | 2 | 16.7% (2) | 0 | 0.649 |
| **Sulphite sensitivity, Ever**  | 7.8% (7) | 2 | 16.7% (2) | 0 | 0.286 |
| **COPD, Ever**  | 6.7% (6) | 2 | 0% (0) | 0 | 0.663 |
| **Nasal polyps, Ever**  | 20.9% (18) | 6 | 27.3% (3) | 1 | 0.699 |
| **Nasal (polyps / sinus) surgery, Ever** | 31.3% (26) | 13 | 36.4% (4) | 1 | 0.740 |
| **Urticaria or Angioedema, Ever**  | 13.3% (12) | 2 | 8.3% (1) | 0 | 1.000 |
| **OSA, Ever**  | 4.4% (4) | 2 | 8.3% (1) | 0 | 0.472 |
| **Eczema, Ever**  | 33.0% (30) | 1 | 25.0% (3) | 0 | 0.747 |

Categorical data are presented as proportions and numbers. Continuous data are either presented as Median + Interquartile range (IQR) or Mean + standard deviation (SD). Exacerbations: incidence of exacerbations requiring OCS / increase in maintenance OCS. AHE: acute healthcare encounters, which include Emergency department/ hospital admissions. PBE: peripheral blood eosinophils. µL: microliter. ACQ6: Asthma Control Questionnaire 6. FENO: fractional exhaled nitric oxide. ppb: parts per billion. OCS: oral corticosteroids; mg: milligrams. FEV1: forced expiratory volume in one second. BMI: Body mass index. GORD: Gastro-oesophageal reflux disease. SPT: skin prick test. sIgE: specific IgE. ICU: intensive care unit. ABPA: allergic bronchopulmonary aspergillosis. COPD: chronic obstructive pulmonary disease. ILO: intermittent laryngeal obstruction. OSA: obstructive sleep apnea. Unpaired t-tests, Mann-Whitney U test, Chi-square tests, or Fisher’s exact tests were used, where appropriate to calculate P-values.

**Supplementary Table S2: Omalizumab super-responders vs non-super-responders**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Omalizumab Super-responderN= 35, 33.7%** | **Omalizumab Non-super-responder N= 69, 66.3%** |  |
|  | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | **P-value** |
| **Annual rate of exacerbations in the past year, median (IQR)**  | 6 (2) | 0 | 4 (4) | 2 | **0.029** |
| **Annual rate of AHE in the past year, median (IQR)**  | 0 (1) | 3 | 1 (2) | 6 | 0.370 |
| **Maximum IgE in the past year, median (IQR) - kU/L**  | 242.00 (350.85) | 2 | 259 (409.1) | 2 | 0.603 |
| **Maximum PBE count in the past year, median (IQR) -cells/µL**  | 200 (200) | 1 | 300 (400) | 8 | 0.863 |
| **Baseline ACQ6, mean (SD)**  | 3.03 (1.01) | 6 | 2.89 (1.37) | 19 | 0.624 |
| **Baseline FENO, median (IQR) - ppb**  | 36.00 (41) | 8 | 27.50 (38.65) | 19 | 0.224 |
| **Baseline Maintenance OCS dose, median (IQR) - mg**  | 10 (21) | 0 | 10 (10) | 1 | 0.962 |
| **Baseline Clinic FEV1%, mean (SD)**  | 67.84 (18.39) | 4 | 66.51 (21.68) | 2 | 0.768 |
| **BMI, median (IQR) - kgm-2**  | 31.4 (7.2) | 0 | 29.90 (10.9) | 0 | 0.380 |
| **Age of asthma diagnosis, median (IQR) - y** | 6.5 (18) | 1 | 13 (31) | 3 | 0.118 |
| **Age at study, mean (SD) - y** | 52 (15.5) | 0 | 52 (15) | 0 | 0.952 |
|  | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **P-value** |
| **Multiple (>1) AHE in the past year, Yes** | 21.9% (7) | 3 | 34.9% (22) | 6 | 0.192 |
| **On Maintenance OCS at baseline, Yes** | 14.3% (5) | 0 | 65.2% (45) | 0 | **<0.001** |
| **Adult-onset asthma, Yes**  | 26.5% (9) | 1 | 42.4% (28) | 3 | 0.118 |
| **Sex, Male**  | 40.0% (14) | 0 | 29.0% (20) | 0 | 0.276 |
| **Ethnicity, White**  | 91.4% (32) | 0 | 87.0% (60) | 0 | 0.747 |
| **Rhinitis, Ever**  | 67.9% (19) | 7 | 77.6% (45) | 11 | 0.333 |
| **GORD, Ever**  | 62.9% (22) | 0 | 64.7% (44) | 1 | 0.853 |
| **Smoking history, Ever**  | 45.7% (16) | 0 | 42.0% (29) | 0 | 0.720 |
| **Obesity (BMI≥30kgm-2), Ever**  | 62.9% (22) | 0 | 47.8% (33) | 0 | 0.147 |
| **ICU admission for asthma, Ever**  | 17.1% (6) | 0 | 33.8% (23) | 1 | 0.075 |
| **Intubation for asthma, Ever**  | 14.3% (5) | 0 | 14.7% (10) | 1 | 0.954 |
| **Dysfunctional breathing, Ever**  | 42.4% (14) | 6 | 55.4% (36) | 4 | 0.225 |
| **ILO, Ever**  | 20.0% (6) | 5 | 19.4% (12) | 7 | 0.942 |
| **Depression, Ever**  | 17.2% (5) | 6 | 39.3% (24) | 8 | **0.036** |
| **Anxiety, Ever**  | 16.7% (5) | 5 | 38.3% (23) | 9 | **0.036** |
| **Bronchiectasis, Ever**  | 11.8% (4) | 1 | 16.2% (11) | 1 | 0.553 |
| **Salicylate sensitivity, Ever**  | 29.4% (10) | 1 | 35.3% (24) | 1 | 0.552 |
| **ABPA, Ever**  | 11.8% (4) | 1 | 13.2% (9) | 1 | 1.000 |
| **Sulphite sensitivity, Ever**  | 8.8% (3) | 1 | 8.8% (3) | 1 | 1.000 |
| **COPD, Ever**  | 2.9% (1) | 1 | 7.4% (5) | 1 | 0.661 |
| **Nasal polyps, Ever**  | 25.8% (8) | 4 | 19.7% (13) | 3 | 0.496 |
| **Nasal (polyps / sinus) surgery, Ever** | 37.9% (11) | 6 | 29.2% (19) | 4 | 0.403 |
| **Urticaria or Angioedema, Ever**  | 11.8% (4) | 1 | 13.2% (9) | 1 | 1.000 |
| **OSA, Ever**  | 5.9% (2) | 1 | 4.4% (3) | 1 | 1.000 |
| **Eczema, Ever**  | 38.2% (13) | 1 | 29.0% (20) | 0 | 0.344 |

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**Supplementary Table S3 –Mepolizumab responders vs non-responders**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Mepolizumab responder N=43, 74.1%** | **Mepolizumab non-responder N=15, 25.9%** |  |
|  | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | **P-value**  |
| **Annual rate of exacerbations in the past year, median (IQR)**  | 4 (5) | 1 | 6 (7) | 1 | 0.310 |
| **Annual rate of AHE in the past year, median (IQR)**  | 0 (1) | 2 | 1 (4) | 1 | **0.020** |
| **Maximum PBE count in the past year, median (IQR) - cells/µL** | 500 (500) | 0 | 500 (300) | 0 | 0.650 |
| **Baseline ACQ6, mean (SD)**  | 2.33 (1.27) | 2 | 4 (0.94) | 1 | **<0.001** |
| **Baseline FENO, median (IQR) - ppb**  | 37 (46.5) | 2 | 22 (60) | 1 | 0.280 |
| **Baseline Maintenance OCS dose, median (IQR) - mg**  | 10 (6) | 0 | 17 (25) | 0 | **0.030** |
| **Baseline Clinic FEV1 %, mean (SD)** | 67% (20.1) | 1 | 64.5 (23.37) | 1 | 0.700 |
| **Baseline HADS, median (IQR)**  | 9 (5) | 6 | 12 (11.5) | 2 | 0.120 |
| **Baseline AQLQ, mean (SD)**  | 4.53 (1.19) | 7 | 3.57 (1.19) | 3 | **0.021** |
| **BMI, median (IQR) - kgm-2**  | 29.1 (11.5) | 0 | 28.2 (12.3) | 0 | 0.540 |
| **Age of asthma diagnosis, median (IQR) - y** | 33.5 (40.5) | 1 | 18 (36) | 0 | 0.498 |
| **Age at study, mean (SD) - y** | 61(16) | 0 | 64 (15) | 0 | 0.517 |
|  | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **P-value** |
| **Multiple (>1) AHE in the past year, Yes**  | 9.8% (4) | 2 | 42.9% (6) | 1 | **0.012** |
| **On Maintenance OCS at baseline, Yes**  | 69.8% (30) | 0 | 80.0% (11) | 0 | 1.000 |
| **Adult-onset asthma, Yes**  | 61.9% (26) | 1 | 53.3% (8) | 0 | 0.561 |
| **Sex, Male**  | 58.1% (25) | 0 | 53.3% (8) | 0 | 0.746 |
| **Ethnicity, White**  | 90.7% (39) | 0 | 100.0% (15) | 0 | 0.407 |
| **Rhinitis, Ever**  | 68.3% (28) | 2 | 73.3% (11) | 0 | 1.000 |
| **GORD, Ever**  | 61.9% (26) | 1 | 80.0% (12) | 0 | 0.339 |
| **Smoking history, Ever**  | 53.5% (23) | 0 | 60.0% (9) | 0 | 0.662 |
| **Atopy (SPT /sIgE positive)**  | 51.2% (22) | 0 | 53.3% (8) | 0 | 0.885 |
| **Obesity (BMI≥30kgm-2), Ever**  | 41.9% (18) | 0 | 40.0% (6) | 0 | 0.900 |
| **ICU admission for asthma, Ever**  | 37.2% (16) | 0 | 26.7% (4) | 0 | 0.460 |
| **Intubation for asthma, Ever** | 9.3% (4) | 0 | 20.0% (3) | 0 | 0.360 |
| **Dysfunctional breathing, Ever**  | 31.7% (13) | 2 | 53.3% (8) | 0 | 0.139 |
| **ILO, Ever**  | 7.7% (3) | 4 | 20.0% (3) | 0 | 0.331 |
| **Depression, Ever**  | 19.1% (8) | 1 | 46.7% (7) | 0 | **0.037** |
| **Anxiety, Ever**  | 20.0% (8) | 3 | 40.0% (6) | 0 | 0.169 |
| **Bronchiectasis, Ever**  | 18.6% (8) | 0 | 20.0% (3) | 0 | 1.000 |
| **Salicylate sensitivity, Ever**  | 18.6% (8) | 0 | 6.7% (1) | 0 | 0.422 |
| **ABPA, Ever**  | 14.0% (6) | 0 | 13.3% (2) | 0 | 1.000 |
| **Sulphite sensitivity, Ever**  | 11.6% (5) | 0 | 0.0% (0) | 0 | 0.326 |
| **COPD, Ever**  | 9.3% (4) | 0 | 13.3% (2) | 0 | 0.643 |
| **Nasal polyps, Ever**  | 37.5% (15) | 3 | 21.4% (3) | 1 | 0.339 |
| **Nasal (polyps / sinus) surgery, Ever**  | 35.7% (15) | 1 | 28.6% (4) | 1 | 0.751 |
| **Urticaria or Angioedema, Ever**  | 7.0% (3) | 0 | 6.7% (1) | 0 | 1.000 |
| **OSA, Ever**  | 4.7% (2) | 0 | 13.33% (2) | 0 | 0.273 |
| **Eczema, Ever**  | 25.6% (11) | 0 | 26.7% (4) | 0 | 1.000 |

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**Supplementary Table S4 –Mepolizumab super-responders vs non-super-responders**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Mepolizumab super-responderN=11, 19%** | **Mepolizumab non-super-responderN=47, 81%** |  |
|  | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | **P-value**  |
| **Annual rate of exacerbations in the past year, median (IQR)**  | 7 (5) | 0 | 4 (5) | 1 | **0.010** |
| **Annual rate of AHE in the past year, median (IQR)**  | 0 (1.75) | 1 | 0 (1) | 2 | 0.789 |
| **Maximum PBE count in the past year, median (IQR) - cells/µL** | 500 (400) | 0 | 500 (500) | 0 | 0.688 |
| **Baseline ACQ6, mean (SD)**  | 1.93 (1.33) | 1 | 3.03 (1.24) | 2 | **0.016** |
| **Baseline FENO, median (IQR) - ppb**  | 46 (49) | 0 | 35.5 (51) | 3 | 0.705 |
| **Baseline Maintenance OCS dose, median (IQR) - mg**  | 10 (22.5) | 0 | 10 (10) | 0 | 0.893 |
| **Baseline Clinic FEV1 %, mean (SD)** | 79.73 (19.97) | 0 | 63.07 (19.84) | 2 | **0.016** |
| **Baseline HADS, median (IQR)**  | 8 (13.5) | 1 | 10.5 (9.5) | 7 | 0.542 |
| **Baseline AQLQ, mean (SD)**  | 5.16 (1.40) | 2 | 4.09 (1.13) | 8 | **0.018** |
| **BMI, median (IQR) - kgm-2**  | 25.1 (5) | 0 | 29.9 (12.3) | 0 | **0.009** |
| **Age of asthma diagnosis, median (IQR) - y** | 37.5 (32) | 1 | 24 (41) | 0 | 0.413 |
| **Age at study, mean (SD) - y** | 62 (16) | 0 | 58 (16) | 0 | 0.482 |
|  | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **P-value** |
| **Multiple (>1) AHE in the past year, Yes**  | 20.0% (2) | 1 | 17.8% (8) | 2 | 1.000 |
| **On Maintenance OCS at baseline, Yes**  | 45.5% (5) | 0 | 76.6% (36) | 0 | 0.064 |
| **Adult-onset asthma, Yes**  | 80.0% (8) | 1 | 55.3% (26) | 0 | 0.178 |
| **Sex, Male**  | 54.5% (6) | 0 | 57.4% (27) | 0 | 1.000 |
| **Ethnicity, White**  | 100% (11) | 0 | 91.5% (43) | 0 | 0.570 |
| **Rhinitis, Ever**  | 80.0% (8) | 1 | 68.9% (31) | 2 | 0.706 |
| **GORD, Ever**  | 54.5% (6) | 0 | 69.6% (32) | 1 | 0.478 |
| **Smoking history, Ever**  | 36.4% (4) | 0 | 59.6% (28) | 0 | 0.193 |
| **Atopy (SPT /sIgE positive)**  | 27.3% (3) | 0 | 57.4% (27) | 0 | 0.071 |
| **Obesity (BMI≥30kgm-2), Ever**  | 9.1% (1) | 0 | 48.9% (23) | 0 | **0.019** |
| **ICU admission for asthma, Ever**  | 27.3% (3) | 0 | 36.2% (17) | 0 | 0.731 |
| **Intubation for asthma, Ever** | 0% (0) | 0 | 14.9% (7) | 0 | 0.334 |
| **Dysfunctional breathing, Ever**  | 30.0% (3) | 1 | 39.1% (18) | 1 | 0.727 |
| **ILO, Ever**  |  0% (0) | 1 | 13.6 (6) | 3 | 0.401 |
| **Depression, Ever**  | 20.0% (2) | 1 | 28.3% (13) | 1 | 0.713 |
| **Anxiety, Ever**  | 11.1% (1) | 2 | 28.3% (13) | 1 | 0.421 |
| **Bronchiectasis, Ever**  | 0% (0) | 0 | 23.4% (11) | 0 | 0.182 |
| **Salicylate sensitivity, Ever**  | 18.2% (2) | 0 | 14.9% (7) | 0 | 1.000 |
| **ABPA, Ever**  | 0% (0) | 0 | 17.0% (8) | 0 | 0.284 |
| **Sulphite sensitivity, Ever**  | 9.1% (1) | 0 | 8.5% (4) | 0 | 1.000 |
| **COPD, Ever**  | 9.1% (1) | 0 | 10.6% (5) | 0 | 1.000 |
| **Nasal polyps, Ever**  | 50.0% (5) | 1 | 29.5% (13) | 3 | 0.273 |
| **Nasal (polyps / sinus) surgery, Ever**  | 45.5% (5) | 0 | 31.1% (14) | 2 | 0.481 |
| **Urticaria or Angioedema, Ever**  | 0% (0) | 0 | 8.5% (4) | 0 | 0.570 |
| **OSA, Ever**  | 0% (0) | 0 | 8.5% (4) | 0 | 0.570 |
| **Eczema, Ever**  | 27.3% (3) | 0 | 25.5% (12) | 0 | 1.000 |

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**Supplementary Table S5: Baseline characteristics of combined biologic non-responders vs SNB and responders**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Combined non-responder group, N=27 (A)** | **Omalizumab responder, N=92 (B)** | **Mepolizumab responder, N=43 (C)** | **Severe asthma, non-biologic group, N=178 (D)** | **P values** |
|  | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | Mean (SD) / Median (IQR) | Missing | **A vs B** | **A vs C** | **A vs D** |
| **Annual rate of exacerbations in the past year, median (IQR)** a,b | 4 (5)  | 2 | 5 (2)  | 1 | 4 (5)  | 1 | 5 (3)  | 32 | 0.526 | 0.864 | 0.978 |
| **Annual rate of AHE in the past year, median (IQR)** a,b | 1 (3)  | 1 | 0 (2)  | 8 | 0 (1)  | 2 | 0 (1)  | 1 | 0.095 | **0.002** | **0.028** |
| **Maximum PBE count in the past year, median (IQR) - cells/µL** a,b | 400 (400)  | 2 | 200 (400) | 7 | 500 (500)  | 0 | 200 (300)  | 49 | **0.005** | 0.178 | **<0.001** |
| **Baseline ACQ6, median (IQR)** b,c | 3.67 (1.26)  | 6 | 3 (1.83)  | 20 | 2.33 (2.27)  | 2 | 3 (1.8)  | 11 | **0.036** | **<0.001** | **0.017** |
| **Baseline FENO, median (IQR) – ppb** b,c | 22 (59.6)  | 4 | 29.5 (37)  | 24 | 37 (46.5)  | 2 | 16.85 (24.65)  | 50 | 0.514 | 0.129 | 0.383 |
| **Baseline Clinic FEV1 %, mean (SD)** b,c | 61.64 (21.75)  | 1 | 68.13 (20.49) | 6 | 67% (20.1)  | 1 | 76.78 (23.37)  | 57 | 0.483 | 0.909 | **0.003** |
| **BMI, median (IQR) -kgm-2**  | 30.6 (15.9) | 0 | 30.36 (5.99) | 0 | 29.1 (11.5) | 0 | 30.8 (10.8) | 3 | 0.194 | 0.160 | 0.469 |
| **Age at asthma diagnosis, median (IQR) - y**  | 12 (31) | 0 | 11 (25.5) | 3 | 33.5 (40.5) | 1 | 20 (35) | 9 | 0.627 | **0.032** | 0.355 |
| **Age, median (IQR) - y** | 54 (28) | 0 | 53 (20.5) | 0 | 61 (19) | 0 | 54.5 (25) | 0 | 0.871 | 0.110 | 0.997 |
|  | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **Percentage (N)** | Missing | **A vs B** | **A vs C** | **A vs D** |
| **Multiple (>1) AHE in the past year, Yes** a,b | 48% (12)  | 2 | 27.4% (23)  | 8 | 9.8% (4)  | 2 | 24.3% (43)  | 5 | 0.053 | **0.001** | **<0.001** |
| **On maintenance OCS at baseline, Yes** b,c | 66.7% (18)  | 0 | 46.7% (43)  | 0 | 69.8% (30)  | 0 | 30.6% (53)  | 1 | 0.069 | 0.797 | **0.013** |
| **Adult-onset asthma**, **Yes** | 38.5% (10) | 0 | 39.3% (35) | 1 | 61.9% (26) | 1 | 52.7% (89) | 9 | 1.000 | 0.060 | 0.178 |
| **Sex, Male** | 33.3% (9) | 0 | 35.9% (33) | 0 | 58.1% (25) | 0 | 29.8% (53) | 0 | 1.000 | **0.043** | 0.822 |
| **Ethnicity, White** | 92.6% (25) | 0 | 89.1% (82) | 0 | 90.7% (39) | 0 | 94.9% (169) | 0 | 0.732 | 1.000 | 0.642 |
| **Rhinitis, Ever**  | 80.8% (21) | 1 | 73.0% (54) | 22 | 68.3% (28) | 2 | 60.1% (95) | 10 | 0.430 | 0.262 | **0.043** |
| **GORD, Ever**  | 73.1% (19) | 1 | 64.1% (59) | 0 | 61.9% (26) | 1 | 65.3% (111) | 8 | 0.485 | 0.344 | 0.434 |
| **Smoking, Ever**  | 51.9% (14) | 0 | 43.5% (40) | 0 | 53.5% (23) | 0 | 47.5% (84) | 1 | 0.442 | 0.894 | 0.670 |
| **Atopy (SPT /sIgE positive)**  | 74.0% (20) | 0 | 100% (92) | 0 | 51.2% (22) | 0 | 52.8% (94) | 0 | **<0.001** | 0.057 | **0.038** |
| **Obesity (BMI≥30kgm-2), Ever**  | 55.6% (15) | 0 | 50.0% (46) | 0 | 41.9% (18) | 0 | 52.6% (92) | 3 | 0.612 | 0.190 | 0.772 |
| **ICU admission for asthma, Ever**  | 33.3% (9) | 0 | 26.4% (24) | 1 | 37.2% (16) | 0 | 32.6% (58) | 0 | 0.479 | 0.802 | 1.000 |
| **Intubated for Asthma, Ever**  | 18.5% (5) | 0 | 14.3% (13) | 1 | 9.3% (4) | 0 | 17.4% (31) | 0 | 0.591 | 0.292 | 1.000 |
| **Dysfunctional breathing, Ever**  | 59.3% (16) | 0 | 48.8% (42) | 6 | 31.7% (13) | 2 | 55.1% (92) | 11 | 0.345 | **0.025** | 0.686 |
| **ILO, Ever**  | 25.9% (7) | 0 | 17.5% (14) | 12 | 7.7% (3) | 4 | 13.2% (21) | 19 | 0.340 | 0.077 | 0.140 |
| **Depression, Ever**  | 48% (12) | 2 | 30.4% (24) | 13 | 19.1% (8) | 1 | 42.8% (68) | 19 | 0.107 | **0.012** | 0.624 |
| **Anxiety, Ever**  | 50% (13) | 1 | 26.6% (21) | 13 | 20.0% (8) | 3 | 38.0% (60) | 19 | **0.027** | **0.011** | 0.245 |
| **Bronchiectasis, Ever**  | 18.5% (5) | 0 | 14.4% (13) | 2 | 18.6% (8) | 0 | 14.2% (25) | 2 | 0.560 | 1.000 | 0.563 |
| **Salicylate sensitivity, Ever**  | 18.5% (5) | 0 | 33.3% (30) | 2 | 18.6% (8) | 0 | 27.8% (49) | 2 | 0.140 | 1.000 | 0.307 |
| **ABPA, Ever**  | 14.8% (4) | 0 | 12.2% (11) | 2 | 14.0% (6) | 0 | 5.2% (9) | 4 | 0.746 | 1.000 | 0.079 |
| **Sulphite sensitivity, Ever**  | 7.4% (2) | 0 | 7.8% (7) | 2 | 11.6% (5) | 0 | 7.4% (13) | 3 | 1.000 | 0.699 | 1.000 |
| **COPD, Ever**  | 7.4% (2) | 0 | 6.7% (6) | 2 | 9.3% (4) | 0 | 10.8% (19) | 2 | 1.000 | 1.000 | 0.746 |
| **Nasal polyps, Ever**  | 24% (6) | 2 | 20.9% (18) | 6 | 37.5% (15) | 3 | 19% (31) | 15 | 0.743 | 0.258 | 0.591 |
| **Nasal (polyps / sinus) surgery, Ever**  | 32% (8) | 2 | 31.3% (26) | 13 | 35.7% (15) | 1 | 19.3% (31) | 17 | 0.949 | 0.757 | 0.145 |
| **Urticaria or Angioedema, Ever**  | 7.4% (2) | 0 | 13.3% (12) | 2 | 7.0% (3) | 0 | 6.8% (12) | 2 | 0.517 | 1.000 | 1.000 |
| **OSA, Ever**  | 11.1% (3) | 0 | 4.4% (4) | 2 | 4.7% (2) | 0 | 11.5% (20) | 4 | 0.350 | 0.367 | 1.000 |
| **Eczema, Ever**  | 25.9% (7) | 0 | 33.0% (30) | 1 | 25.6% (11) | 0 | 21.6% (38) | 2 | 0.489 | 1.000 | 0.614 |

Categorical data : proportions and numbers. Continuous data: Median + Interquartile range (IQR) or Mean + standard deviation (SD). a: For biologic groups, In the preceding 12 months prior to biologic approval. b: For the non-biologic group,at WATCH enrolment. c: for biologic groups, at baseline biologic visit. Exacerbations: incidence of exacerbations requiring OCS / increase in maintenance OCS. AHE: acute healthcare encounters, which include Emergency department/ hospital admissions. PBE: peripheral blood eosinophils. µL: microlitre. ACQ6: Asthma Control Questionnaire 6. FENO: fractional exhaled nitric oxide. ppb: parts per billion. IgE: immunoglobulin E. kU/L: kilounits per litre. OCS: oral corticosteroids. mg: milligrams. FEV1: forced expiratory volume in one second. Adult-onset: Age of asthma onset ≥18 years GORD: Gastro-oesophageal reflux.disease. SPT: skin prick test. sIgE: specific IgE. ICU: intensive care unit. ILO: intermittent laryngeal obstruction. ABPA: allergic bronchopulmonary aspergillosis. COPD: chronic obstructive pulmonary disease. OSA: obstructive sleep apnoea. The severe asthma, non-biologic (SNB) group is a common comparator group extracted from WATCH. They were participants who either had ≥4 exacerbations or ≥1 AHE or were on maintenance OCS in the past year but did not commence biologic therapy during the study period. Combined non-responders were a combined group of Omalizumab non-responders (N=12) and Mepolizumab non-responders (N=15). Unpaired t-tests, Mann-Whitney U test, Chi-square tests or Fisher’s exact tests were used, where appropriate, to calculate P-values.