ONLINE SUPPLEMENT

Australian Mepolizumab Registry additional methods and results for:

Mepolizumab effectiveness and identification of super-responders in severe asthma (Harvey et al.)

METHODS

Human Research Ethics Committee approval

Ethical approval for the registry was received from the Hunter New England Human Research Ethics Committee (HREC) for centres in New South Wales, Queensland, Victoria and South Australia, and also from the Mater Health Services HREC, Tasmanian Health and Medical HREC and South Metropolitan Health Service HREC.

Multivariate regression analysis

Baseline predictors of ACQ-5 response were evaluated using multiple linear regression. Baseline variables considered for inclusion were patient age, sex, body mass index category (<30 or ≥30 kg/m^2), blood eosinophil count (during 12 months prior), smoking status (ex-/current-smoker or never-smoker), age of asthma onset and atopic status (atopic or non-atopic). Variables for the multivariate models were chosen if the p-value was <0.2 in the linear model. Age, sex, body mass index category, blood eosinophil count and age of asthma onset were included in the multivariate model. Results were considered significant when $p<0.05$.

Sub-group analyses

Clinical responses to mepolizumab treatment [change from baseline in Asthma Control Questionnaire (ACQ-5) score, Asthma Quality of Life Questionnaire – standardised (AQLQ(S)) score and lung function]

were assessed according to patient age of asthma onset (<40 or ≥40 years), atopic status and baseline blood eosinophil level (≤600 or >600 cells/µL).

RESULTS

Respiratory medication use and exemptions

All patients were using an inhaled corticosteroid (ICS) and long-acting beta agonist (LABA), with the exception of 2 patients who were exempted from LABA use due to toxicity/inability to tolerate [median (IQR) (ICS) dose of 2000 (1000,2000) Chlorofluorocarbon-beclomethasone diproprionate (CFC-BDP) equivalents (mcg/day)].

Supplementary table S1: Patient comorbidities at baseline

Comorbidities	**n = 299**
Allergic rhinitis	187 (62.5%)
Gastro-oesophageal Reflux Disease	155 (51.8%)
Obstructive Sleep Apnoea	61 (20.4%)
Vocal Cord Dysfunction	27 (9.0%)
Chronic Obstructive Pulmonary Disease	51 (17.1%)
Bronchiectasis	40 (13.4%)
Nasal Polyps	103 (34.4%)
Osteoporosis	60 (20.1%)
Aspirin sensitivity	36 (12.0%)
Cardiovascular disease	70 (23.4%)
Anaphylaxis	39 (13.0%)
Eczema	61 (20.4%)
Dysfunctional Breathing	2 (0.7%)
Allergic Bronchopulmonary Aspergillosis	25 (8.4%)
Psychiatric disorder (anxiety/depression/other)	86 (28.8%)
Obesity, n=297	136 (45.8%)
Diabetes	38 (12.7%)
Other endocrine disorders	18 (6.0%)

Data presented as n(%).

Supplementary table S2: Serious adverse events recorded during the 12-month follow-up period for patients who commenced mepolizumab.

Serious adverse events	**n=309**
Total number of serious adverse events reported	25 (n=18 patients)
Serious adverse event outcome: Fatal	2/25
Cause of death:	
Acute myocardial infarction	1
Ischaemic heart disease	1
Causality to mepolizumab	
Suspected	0/25
Not suspected	25
Action regarding mepolizumab treatment	
None	20/25
Temporarily adjusted or interrupted	4
Permanently discontinued	1
Reason permanently discontinued:	
Metastatic brain lesion	1
Reasons temporarily adjusted or interrupted:	
Right main pulmonary artery embolus	1
Pneumonia	1
Right middle cerebral artery stroke	1
Symmetrical polyarthralgia	1

Data are reported as n/N events

Supplementary table S3: Baseline characteristics of patients by baseline peripheral blood eosinophil level, and changes from baseline to follow-up with mepolizumab treatment.

		BASELINE BLOOD EOSINOPHILS ≤600/µL	**BASELINE BLOOD EOSINOPHILS >600/µL**	**p-value**
Baseline characteristic	n=309	n=178	n=131	
ACQ-5 score	3.4 (3.0, 4.2)	3.4 (3.0, 4.2)	3.6 (3.0, 4.2)	0.57
FEV_1 % predicted (pre-B2)	56.90 ± 17.78	56.52 ± 18.34	57.45 ± 17.03	0.70
AQLQ(S) mean score	3.78 ± 1.16	3.77 ± 1.18	3.80 ± 1.12	0.83
Maintenance OCS use	144 (47%)	82 (46%)	62 (47%)	0.83
OCS total daily dose*	10 (5.0,12.5)	10.00 (5.00, 12.50)	10.00 (5.00, 12.50)	0.91
Difference from baseline	**Total**	**BASELINE BLOOD EOSINOPHILS ≤600/µL**	**BASELINE BLOOD EOSINOPHILS >600/µL**	**p-value**
3-months	n=299	n=170	n=129	
ACQ-5 mean score	-1.78 ± 1.24	-1.60 ± 1.17	-2.02 ± 1.30	**0.013**
FEV_1 % predicted (pre-B2)	4.73 (-1.38, 11.63)	3.66 (-2.46, 11.85)	6.14 (1.08, 11.63)	0.19
AQLQ(S) mean score	1.18 ± 1.13	1.01 ± 1.08	1.43 ± 1.17	**0.019**
6-months	n=284	n=158	n=126	
ACQ-5 mean score	-2.01 ± 1.18	-1.82 ± 1.06	-2.25 ± 1.27	**0.003**
FEV_1 % predicted (pre-B2)	3.74 (-2.74, 12.03)	2.71 (-3.14, 7.89)	5.97 (-0.31, 13.50)	0.055
AQLQ(S) mean score	1.31 ± 1.25	1.12 ± 1.20	1.56 ± 1.28	**0.026**
12-months	n=225	n=122	n=103	
ACQ-5 mean score	-2.19 ± 1.20	-2.03 ± 1.05	-2.36 ± 1.33	**0.047**
FEV_1 % predicted (pre-B2)	5.50 (-1.11, 13.91)	3.18 (-1.65, 8.84)	8.02 (-0.90, 16.32)	**0.032**
AQLQ(S) mean score	1.54 ± 1.25	1.49 ± 1.19	1.60 ± 1.32	0.64
Difference from baseline	**Total**	**NOT on maintenance OCS + BLOOD EOSINOPHILS ≤600/µL**	**NOT on maintenance OCS + BLOOD EOSINOPHILS >600/µL**	**p-value**
3-months	N=158	N=91	N=67	
ACQ-5 mean score	-1.92 ± 1.23	-1.69 ± 1.19	-2.21 ± 1.24	**0.023**
FEV_1 % predicted (pre-B2)	4.41 (-1.81, 10.51)	2.17 (-2.41, 9.52)	6.48 (2.21, 11.63)	0.078
AQLQ(S) mean score	1.23 ± 1.18	0.95 ± 1.07	1.65 ± 1.24	**0.006**
6-months	N=156	N=88	N=68	
ACQ-5 mean score	-2.14 ± 1.13	-2.01 ± 1.02	-2.32 ± 1.24	0.10
FEV_1 % predicted (pre-B2)	4.24 (-1.03, 11.66)	3.05 (-1.29, 7.55)	5.97 (-0.78, 13.62)	0.27
AQLQ(S) mean score	1.39 ± 1.27	1.25 ± 1.16	1.56 ± 1.38	0.26
12-months	N=124	N=70	N=54	
ACQ-5 mean score	-2.33 ± 1.13	-2.30 ± 1.05	-2.37 ± 1.23	0.75
FEV_1 % predicted (pre-B2)	6.74 (-0.87, 13.87)	3.55 (-0.87, 8.63)	9.87 (2.40, 15.79)	**0.043**
AQLQ(S) mean score	1.58 ± 1.28	1.64 ± 1.16	1.50 ± 1.44	0.66
Difference from baseline	**Total**	**ON maintenance OCS + BLOOD EOSINOPHILS ≤600/µL**	**ON maintenance OCS + BLOOD EOSINOPHILS >600/µL**	**p-value**
3-months	N=141	N=79	N=62	
ACQ-5 mean score	-1.63 ± 1.24	-1.52 ± 1.16	-1.79 ± 1.35	0.26
FEV_1 % predicted (pre-B2)	4.78 (-1.38, 12.89)	4.76 (-2.77, 13.72)	5.59 (-0.61, 11.83)	0.94
AQLQ(S) mean score	1.13 ± 1.08	1.09 ± 1.10	1.20 ± 1.06	0.65

6-months	N=128	N=70	N=58	
ACQ-5 mean score	-1.86 ± 1.22	-1.59 ± 1.09	-2.17 ± 1.30	**0.009**
FEV_1 % predicted (pre-B2)	3.47 (-3.14, 12.62)	1.79 (-4.25, 12.10)	6.06 (1.07, 13.06)	0.11
AQLQ(S) mean score	1.22 ± 1.23	0.95 ± 1.24	1.56 ± 1.16	**0.038**
12-months	N=101	N=52	N=49	
ACQ-5 mean score	-2.01 ± 1.26	-1.66 ± 0.93	-2.35 ± 1.45	**0.007**
FEV_1 % predicted (pre-B2)	3.95 (-1.65, 14.19)	3.03 (-2.18, 11.35)	6.56 (-0.93, 16.39)	0.31
AQLQ(S) mean score	1.49 ± 1.21	1.27 ± 1.23	1.70 ± 1.18	0.20

Baseline data presented as mean±SD, Student's t test, median (IQR), Wilcoxon rank-sum test; n(%), Pearson's chi-squared or Fisher's exact test. Response data presented as mean±SD difference, Two-sample t test, median (IQR) difference, Wilcoxon rank-sum. ACQ: Asthma Control Questionnaire, AQLQ(S): Asthma Quality of Life Questionnaire (standardised), B2: bronchodilator, FEV_1: forced expiratory volume in 1 second. OCS: Oral Corticosteroids. *OCS total daily dose, prednisolone equivalents (mg/day).

Supplementary table S4: Changes from baseline to follow-up with mepolizumab treatment, by sub-group (age of asthma onset, atopic status and baseline body mass index)

Difference from baseline	**Total**	**AGE of ASTHMA ONSET <40 YEARS**	**AGE of ASTHMA ONSET ≥40 YEARS**	**p-value**
6-months	n=252	n=175	n=77	
ACQ-5 mean score	-1.98 ± 1.16	-1.95 ± 1.12	-2.07 ± 1.25	0.44
FEV_1 % predicted (pre-B2)	3.72 (-2.74, 12.16)	4.59 (-2.40, 11.99)	3.17 (-3.79, 16.42)	0.95
AQLQ(S) mean score	1.31 ± 1.25	1.36 ± 1.20	1.19 ± 1.38	0.47
12-months	n=196	n=135	n=61	
ACQ-5 mean score	-2.16 ± 1.18	-2.13 ± 1.16	-2.22 ± 1.25	0.65
FEV1 % predicted (pre-B2)	6.20 (-1.11, 13.91)	4.08 (-1.04, 11.82)	10.00 (-3.09, 15.79)	0.29
AQLQ(S) mean score	1.54 ± 1.26	1.59 ± 1.33	1.41 ± 1.09	0.46
Difference from baseline	**Total**	**NON-ATOPIC**	**ATOPIC**	**p-value**
6-months	n=203	n=58	n=145	
ACQ-5 mean score	-2.02 ± 1.19	-2.00 ± 1.36	-2.03 ± 1.11	0.88
FEV_1 % predicted (pre-B2)	4.26 (-1.27, 11.66)	5.29 (-0.77, 10.93)	3.77 (-2.40, 11.99)	0.55
AQLQ(S) mean score	1.42 ± 1.28	1.40 ± 1.30	1.42 ± 1.28	0.93
12-months	n=163	n=49	n=114	
ACQ-5 mean score	-2.17 ± 1.19	-2.40 ± 1.26	-2.07 ± 1.14	0.10
FEV_1 % predicted (pre-B2)	6.59 (-1.04, 13.91)	6.74 (-0.87, 18.05)	5.12 (-1.99, 12.02)	0.19
AQLQ(S) mean score	1.64 ± 1.27	1.82 ± 1.33	1.55 ± 1.25	0.32
Difference from baseline	**Total**	**BASELINE BMI <35**	**BASELINE BMI ≥35**	**p-value**
6-months	n=274	n=211	n=63	
ACQ-5 mean score	-2.03 ± 1.18	-2.11 ± 1.16	-1.74 ± 1.21	**0.039**
FEV_1 % predicted (pre-B2)	3.72 (-2.74, 11.99)	3.25 (-2.81, 11.99)	4.15 (-1.24, 12.16)	0.93
AQLQ(S) mean score	1.31 ± 1.25	1.40 ± 1.31	1.05 ± 1.00	0.13
12-months	n=216	n=168	n=48	
ACQ-5 mean score	-2.21 ± 1.20	-2.21 ± 1.17	-2.21 ± 1.32	0.98
FEV_1 % predicted (pre-B2)	5.83 (-1.11, 13.91)	6.66 (-1.11, 15.79)	3.42 (-1.08, 9.25)	0.14
AQLQ(S) mean score	1.54 ± 1.25	1.62 ± 1.27	1.27 ± 1.14	0.19

Data presented as mean±SD difference, Two-sample t test, median (IQR) difference, Wilcoxon rank-sum, ACQ: Asthma Control Questionnaire, AQLQ(S): Asthma Quality of Life Questionnaire (standardised), BMI: Body mass index, FEV_1: forced expiratory volume in 1 second. Atopy positive classified by positive skin prick test or Radioallergosorbent test/ImmunoCAP and/or previous omalizumab treatment.

Supplementary table S5. Baseline characteristics of patients by age of asthma onset (<40 or ≥40 years)

	Age of asthma onset < 40 years (n=188)	Age of asthma onset ≥ 40 years (n=86)	p-value
Age	56.36 (45.59, 64.99) (n=188)	67.13 (60.96, 72.60) (n=85)	**<0.001**
Gender (% male)	69 (36.7%)	50 (58.1%)	**<0.001**
Smoking:			**0.034**
Never	123 (65.8%)	45 (52.9%)	
Current	0 (0.0%)	1 (1.2%)	
Ex	64 (34.2%)	39 (45.9%)	
Pack years (ex/current smokers)	12.25 (2.70, 20.00) (n=62)	25.00 (9.00, 39.75) (n=39)	**0.002**
Body Mass Index kg/m^2	29.53 (24.96, 34.89) (n=183)	29.98 (27.13, 34.37) (n=83)	0.64
Atopy	103 (71.5%)	36 (61.0%)	0.21
Asthma duration, years	37.90 (24.32, 51.95) (n=188)	12.28 (4.92, 18.79) (n=85)	**<0.001**
ACQ-5 score	3.40 (2.80, 4.20) (n=186)	3.60 (3.00, 4.20) (n=86)	0.28
Exacerbation history, past year			
Course of OCS required	178 (94.7%)	83 (96.5%)	0.76
Number of OCS courses	4.00 (2.00, 6.00) (n=174)	3.00 (2.00, 5.00) (n=83)	**0.028**
Number of hospital admissions	1.00 (1.00, 2.00) (n=48)	1.00 (1.00, 2.00) (n=26)	0.72
Pre-bronchodilator spirometry			
FEV1 % predicted	56.04 ± 17.60 (n=150)	59.37 ± 17.78 (n=67)	0.20
FVC % predicted	77.57 ± 16.19 (n=150)	83.00 ± 15.83 (n=66)	**0.023**
FEV1/FVC	0.57 ± 0.13 (n=150)	0.56 ± 0.13 (n=66)	0.43
Biomarkers			
Peripheral blood eosinophils, cells/µL	600 (400, 840) (n=185)	590 (380, 880) (n=85)	0.95
IgE, IU/mL	140 (42, 527) (n=131)	139 (70, 264) (n=56)	0.63
FeNO, ppb	32 (18, 61) (n=99)	37 (21, 60) (n=45)	0.55
Asthma triggers			
Seasons	147 (78.2%)	50 (58.1%)	**<0.001**
Exercise	156 (83.0%)	61 (70.9%)	**0.023**
URTI	160 (85.1%)	68 (79.1%)	0.21
Reflux	50 (26.6%)	20 (23.3%)	0.56
Pets	64 (34.0%)	13 (15.1%)	**0.001**
Food	64 (34.0%)	14 (16.3%)	**0.002**
Aspirin	31 (16.5%)	5 (5.8%)	**0.015**
Other	76 (40.4%)	24 (27.9%)	0.046
Comorbidities			
Allergic rhinitis	135 (71.8%)	46 (54.1%)	**0.004**
GORD	105 (55.9%)	40 (47.1%)	0.18
COPD	28 (14.9%)	21 (24.7%)	0.050
Obstructive sleep apnoea	42 (22.3%)	18 (21.2%)	0.83
Bronchiectasis	28 (14.9%)	9 (10.6%)	0.45
Nasal polyps	69 (36.7%)	30 (35.3%)	0.82
Eczema	51 (27.1%)	7 (8.2%)	**<0.001**
Psychiatric disorder	64 (34.0%)	18 (21.2%)	**0.032**
Osteoporosis	45 (23.9%)	11 (12.9%)	**0.037**
Cardiovascular disease	38 (20.2%)	27 (31.8%)	**0.038**
Obesity	88 (48.1%)	41 (49.4%)	0.84

(supplementary table S5 continued from previous page) Data presented as mean±SD, Student's t test, median (IQR), Wilcoxon rank-sum test; n(%), Pearson's chi-squared or Fisher's exact test. Bold-type represents significant difference ($p<0.05$). ACQ: Asthma Control Questionnaire, ATSI: Aboriginal or Torres Strait Islander, BMI: Body Mass Index, COPD: Chronic obstructive pulmonary disease, FEV_1: forced expiratory volume, FVC: forced vital capacity, FeNO; fraction of exhaled nitric oxide, GORD: Gastro-oesophageal Reflux Disease, OCS: oral corticosteroids. Atopy positive classified by positive skin prick test or Radioallergosorbent test/ImmunoCAP and/or previous omalizumab treatment.

Supplementary table S6: Characteristics of patients with non-atopic eosinophilic asthma and atopic eosinophilic asthma prior to commencement of mepolizumab

	Non-atopic eosinophilic asthma (n=65)	Atopic eosinophilic asthma (n=156)	p-value
Age	59.95 (54.49, 69.20) (n=65)	59.10 (46.92, 66.96) (n=156)	0.26
Gender (% male)	23 (35.4%)	72 (46.2%)	0.14
Race:			0.35
White	58 (93.6%)	125 (85.0%)	
Asian	1 (1.6%)	11 (7.5%)	
Pacific Islander	1 (1.6%)	3 (2.0%)	
Other	2 (3.2%)	8 (5.5%)	
Smoking:			0.50
Never	36 (56.3%)	98 (63.6%)	
Current	0 (0.0%)	1 (0.7%)	
Ex	28 (43.7%)	55 (35.7%)	
Pack years (ex/current smokers)	20.00 (12.75, 30.00) (n=27)	12.00 (4.00, 35.00) (n=55)	0.32
Asthma duration, years	24.15 (11.55, 37.75) (n=64)	29.50 (16.40, 48.20) (n=139)	**0.042**
Exacerbation history, past year			
Course of OCS for exacerbation	63 (96.9%)	147 (94.2%)	0.51
Number of OCS courses	4.00 (3.00, 7.00) (n=62)	3.00 (2.00, 6.00) (n=144)	0.060
Number of hospital admissions	1.00 (1.00, 4.00) (n=16)	1.00 (1.00, 3.00) (n=48)	0.88
Pre-bronchodilator spirometry			
FEV_1 % predicted	58.27 ± 18.60 (n=52)	55.57 ± 17.74 (n=125)	0.36
FVC % predicted	78.08 ± 16.18 (n=51)	77.50 ± 17.11 (n=125)	0.84
FEV_1/FVC	0.58 ± 0.14 (n=51)	0.57 ± 0.13 (n=125)	0.41
Asthma control			
ACQ-5 score	3.80 (3.00, 4.40) (n=65)	3.40 (3.00, 4.20) (n=154)	0.084
Biomarkers			
Peripheral Blood eosinophils, cells/µL	500 (400, 850) (n=64)	545 (400, 800) (n=154)	0.92
IgE, IU/mL	77.5 (18.0, 158.0) (n=54)	213.0 (76.0, 717.0) (n=113)	**<0.001**
FeNO, ppb	43.0 (21.0, 102.0) (n=31)	29.5 (17.0, 59.7) (n=86)	0.10
Comorbidities			
Gastro-oesophageal reflux disease	41 (63.1%)	74 (48.4%)	0.047
Bronchiectasis	5 (7.7%)	26 (17.0%)	0.090
Nasal polyps	21 (32.3%)	49 (32.0%)	0.97
ABPA	0 (0.0%)	22 (14.4%)	**<0.001**
Respiratory medication use			
ICS total daily dose (CFC-BDP equivalent, mcg/day)	2000.0 (2000.0, 2500.0) (n=65)	2000.0 (1000.0, 2000.0) (n=155)	0.070
Maintenance OCS use	30 (46.2%)	69 (44.2%)	0.79
OCS total daily dose, prednisone equivalents mg/per day	7.25 (5.00, 10.00) (n=30)	10.00 (5.00, 12.50) (n=69)	0.26
Total number of respiratory medications	4.0 (3.0, 5.0) (n=65)	4.0 (3.0, 5.0) (n=156)	0.88

ICS single device	27 (41.5%)	33 (21.2%)	**0.002**
ICS/LABA combination device	59 (90.8%)	145 (92.9%)	0.58
Theophylline	8 (12.3%)	5 (3.2%)	**0.009**
LAMA/LABA combination device	8 (12.3%)	4 (2.6%)	**0.007**
Antifungal	0 (0.0%)	8 (5.1%)	0.11
Macrolide	2 (3.1%)	24 (15.4%)	**0.010**

(Supplementary table S6 continued from previous page) Data presented as mean±SD, Student's t test; median (IQR), Wilcoxon rank-sum test; n(%), Pearson's chi-squared or Fisher's exact test. Bold-type represents significant difference ($p<0.05$). ABPA: Allergic bronchopulmonary aspergillosis, ACQ: Asthma Control Questionnaire, CFC-BDP: Chlorofluorocarbon-beclomethasone diproprionate, BMI: Body Mass Index, FEV_1: forced expiratory volume, FVC: forced vital capacity, FeNO; fraction of exhaled nitric oxide, ICS: Inhaled corticosteroids, LABA: Long-acting beta agonist, LAMA: Long-acting muscarinic antagonist, OCS: oral corticosteroids. Atopy positive classified by positive skin prick test or Radioallergosorbent test/ImmunoCAP and/or previous omalizumab treatment.

Supplementary table S7: Baseline characteristics of patients identified as mepolizumab responders and treatment failures

	Responders (n=260)	Treatment failures (n=42)	p-value
Age	59.30 (50.29, 68.12)	62.98 (51.81, 69.56)	0.36
Gender (% male)	110 (42.3%)	19 (45.2%)	0.72
Smoking:			0.79
Never	159 (61.6%)	23 (59.0%)	
Current	2 (0.8%)	0 (0.0%)	
Ex	97 (37.6%)	16 (41.0%)	
Pack years (ex/current smokers)	15.00 (4.00, 30.00)	20.00 (9.00, 25.00)	0.95
Body Mass Index kg/m^2	29.41 (25.22, 34.37)	29.52 (26.93, 35.85)	0.80
Atopy	133 (71.1%)	21 (67.7%)	0.70
Asthma duration, years	30.10 (14.72, 46.56)	21.47 (10.19, 42.33)	0.14
Exacerbation history, past year			
Course of OCS for exacerbation	247 (95.0%)	41 (97.6%)	0.70
Number of OCS courses	3.00 (2.00, 6.00)	3.00 (2.00, 5.00)	0.76
Number of hospital admissions	1.00 (1.00, 2.00)	1.00 (1.00, 5.00)	0.33
Pre-bronchodilator spirometry			
FEV_1 % predicted	56.75 ± 17.51	56.06 ± 19.71	0.83
FVC % predicted	79.25 ± 16.41	74.02 ± 18.85	0.095
FEV_1/FVC	0.56 ± 0.13	0.61 ± 0.15	0.055
Asthma control			
ACQ-5 score	3.40 (3.00, 4.20)	3.80 (3.00, 4.40)	0.48
Biomarkers			
Peripheral Blood eosinophils, cells/µL	600 (400, 870)	400 (300, 690)	**<0.001**
IgE, IU/mL	129.0 (46.0, 416.0)	204.5 (91.0, 791.5)	0.11
FeNO, ppb	35.0 (18.5, 60.0)	32.0 (20.2, 64.2)	0.53
Comorbidities			
Allergic rhinitis	160 (63.5%)	22 (55.0%)	0.30
GORD	129 (51.2%)	22 (55.0%)	0.65
COPD	42 (16.7%)	8 (20.0%)	0.60
Obstructive sleep apnoea	52 (20.6%)	9 (22.5%)	0.79
Bronchiectasis	37 (14.7%)	3 (7.5%)	0.32
Nasal polyps	93 (36.9%)	8 (20.0%)	**0.037**
Eczema	49 (19.4%)	10 (25.0%)	0.42
Psychiatric disorder	73 (29.0%)	11 (27.5%)	0.85
Osteoporosis	52 (20.6%)	7 (17.5%)	0.65
Cardiovascular disease	56 (22.2%)	12 (30.0%)	0.28
Obesity	115 (45.8%)	17 (43.6%)	0.80
Respiratory medication use			
ICS total daily dose (CFC-BDP equivalent, mcg/day)	2000 (1000, 2000)	2000 (1000, 2000)	0.70
Maintenance OCS use	114 (43.8%)	27 (64.3%)	**0.014**
OCS total daily dose, prednisolone equivalents mg/day	7.50 (5.00, 12.50)	10.00 (5.00, 15.00)	0.24

Data presented as mean±SD, Student's t test; median (IQR), Wilcoxon rank-sum test; n(%), Pearson's chi-squared or Fisher's exact test. Bold-type represents significant difference (p<0.05). PBS responders were

patients with a successful first continuation of PBS-subsidised mepolizumab treatment (ACQ-5 score reduction of at least 0.5 from baseline or at least 25% reduction in oral corticosteroid dose without deterioration of ACQ-5) at 6-months post-commencement. Treatment failures were patients who did not have a successful first continuation of PBS-subsidised mepolizumab treatment. ACQ: Asthma Control Questionnaire, CFC-BDP: Chlorofluorocarbon-beclomethasone diproprionate, FEV_1: forced expiratory volume, FVC: forced vital capacity, FeNO; fraction of exhaled nitric oxide, ICS: Inhaled corticosteroids, PBS: Australian Government's Pharmaceutical Benefit Scheme. Atopy positive classified by positive skin prick test or Radioallergosorbent test/ImmunoCAP and/or previous omalizumab treatment.

Supplementary table S8: Clinical response in super-responders [responders with top 25% of ACQ-5 change and patients who achieved well-controlled asthma symptoms (ACQ <1.0)]

	6-month assessment				
	All PBS responders	**Super-responders:** Top 25% of ΔACQ5 from baseline group	Bottom 25% of ΔACQ5 from baseline group	**Super-responders:** Well controlled ACQ-5 <1.0 group	Uncontrolled ACQ-5 >1.5 group
SYMPTOMS	n=252	n=61	n=70	n=79	n=111
ΔACQ-5 improvement Median (IQR)	-2.0 (-1.4 , -3.0)	-3.4 (-3.2, -4.0)	-1.0 (-0.6, -1.2)	-3.0 (-2.4 , -3.6)	-1.4 (-1.0, -2.0)
ΔACQ-5 improvement Mean ± SD	-2.15 ± 1.08	-3.6 ± 0.64	-0.93 ± 0.36	-3.05 ± 1.00	-1.53 ± 0.74
EXACERBATIONS	n=260	n=61	n=70	n=79	n=111
Patients free of exacerbations requiring OCS, n(%)	141 (54.2%)	43 (70.5%)	30 (42.9%)	53 (67.1%)	46 (41.4%)
OCS USE	n=260	n=61	n=70	n=79	n=111
Patients free of maintenance OCS use, n(%)	182 (70.0%)	47 (77.0%)	43 (61.4%)	62 (78.5%)	69 (62.2%)

PBS responders were patients with a successful first continuation of PBS-subsidised mepolizumab treatment (ACQ-5 score reduction of at least 0.5 from baseline or at least 25% reduction in oral corticosteroid dose without deterioration of ACQ-5) at 6-months post-commencement. ACQ: Asthma Control Questionnaire, OCS: Oral corticosteroids, PBS: Australian Government's Pharmaceutical Benefit Scheme.

Supplementary table S9: Comparison of baseline characteristics and response to mepolizumab in AMR patients and regulatory trial participants.

Baseline demographic and clinical characteristics	**AMR**	**MENSA active arm only** (ref 9)	**MUSCA active arm only** (ref 11)	**p-value AMR vs MENSA**	**p-value AMR vs MUSCA**
	n = 309	n = 194	n = 274		
Age, years	58.0 ± 14.2 59.55 (49.99,68.28)	51	49.8 ± 14.0	*not able to compare*	**p<0.001**
Female sex (%)	57.6	60	54		
Body mass index	30.7 ± 7.3 29.45 (25.30,34.46)	27.6 ± 6.2	28.5 ± 6.6	**p<0.001**	**p<0.001**
Ex-smokers (%)*	38	26 (ex>10 pack years)	26 (ex>10 pack years)	*not able to compare*	*not able to compare*
Asthma duration, years	30.7 ± 19.6 27.52 (13.30,46.08) n =273	20.5 ± 12.9	19.5 ± 14.7	**p<0.001**	**p<0.001**
Maintenance OCS use (%)	47	27	23	**p<0.001**	**p<0.001**
FEV_1 % of predicted, pre-bronchodilator	56.9 ±17.8, n =233	59.3 ± 17.5	55.5 ± 14.4	p=0.14	p=0.3
FEV_1 % of BDR	11.77 ± 15.45, n=204	27.9 ± 24.0	22.0 ± 23.2	**p<0.001**	**p<0.001**
ACQ-5	3.58 ± 0.91 3.4 (3.0,4.2), n =306	2.26 ± 1.27	2.2 ± 1.1	**p<0.001**	**p<0.001**
Peripheral blood eosinophils, cells/µL	693 ± 469 590 (400, 830)	290 ± 1050	300	**p<0.001**	*not able to compare*
Severe exacerbations requiring OCS, 12 months prior	4.5 ± 4.1 3.0 (2.0,6.0)	3.8 ± 2.7	2.9 ± 1.9	**p=0.021**	**p<0.001**
Response to mepolizumab (change from baseline)	**AMR 100mg SC all patients**	**MENSA 100mg SC active arm only**	**MUSCA 100mg SC active only**	**p-value AMR vs MENSA**	**p-value AMR vs MUSCA**
	6-8 months	**32 weeks**	**24 weeks**		
ACQ-5 score	-2.01 ± 1.18 n =268	-0.94 ± 0.98 n =194	-0.8 ± 0.16 n =266	**p<0.001**	**p<0.001**

AMR data presented as median (IQR) and mean±SD or %/n. MENSA and MUSCA data are presented as mean±SD or %/n. Mean±SD compared by independent samples t-test and categorical data compared using Pearson's chi-squared test. *Unable to compare smoking status due to definitional differences between AMR and MENSA/MUSCA. Bold-type represents significant difference (p<0.05). ACQ: Asthma Control Questionnaire, BDR: bronchodilator reversibility, FEV_1: forced expiratory volume, FeNO; fraction of exhaled nitric oxide, OCS: oral corticosteroids.