SUPPLEMENTAL APPENDIX

Exclusion criteria

- Current smoker or smoking cessation within the last 6 months
- Severe exacerbation or alteration to asthma therapy within 4 weeks prior to Visit 1
- Eligible for commencing Omalizumab (according to current PBS criteria), or currently within the first 6 months of commencing Omalizumab.
- Eligible for commencing Mepolizumab or currently within the first 6 weeks of commencing Mepolizumab
- Other medical comorbidity or research study requiring chronic systemic corticosteroid (for example rheumatologic conditions, adrenal insufficiency, etc.)
- Inability to take oral corticosteroid

Co-morbid conditions such as upper airway dysfunction, reflux, rhinitis and OSA are not exclusion criteria, provided they have been assessed and their management optimised according to current clinical guidelines prior to randomisation.

Exacerbation Definition

Protocol definition of asthma exacerbation:

An asthma exacerbation will be defined as a worsening of asthma control (characterized by a progressive increase in symptoms and progressive decrease in lung function requiring a change in treatment). Severe exacerbations will require systemic glucocorticoids or an increase in the dose of regular systemic glucocorticoids for at least 3 days. [18]

For episodes where two periods of exacerbation (i.e. worsening symptoms, hospitalization or use of corticosteroids for the purposes of treating an asthma exacerbation) occur consecutively, they will be counted as two separate events if separated by at least a week.

Supplemental Table 1: Study Visit Schedule

Participants were assessed at a total of 14 study clinic visits over a 52 week period for the following:

Study Visit	0 Screening	1 Randomisation	2	3	4	5	6	7	8*	9	10*	11	12*	13
Study week	**-4**	**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**
Informed consent	X													
Medication history and adherence	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Inclusion /exclusion criteria	X	X												
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Randomisation		X												
Clinician consultation		X				X				X				X
Spirometry	X	X	X	X	X	X	X	X		X		X		X
FeNO	X	X	X	X	X	X	X	X		X		X		X
ACQ-6; AQLQ	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Induced sputum sample	X													X
Review Asthma Action Plan	X													
Outcome Assessment		x	x	x	x	x	x	x	X	x	X	x	X	x
Serum and Peripheral blood eosinophils (FBC)	X	x	x	x	x	x	x	X		x		x		x

*Denotes telephone visit.

Supplemental Table 2: Instructions for OCS titration based on biomarker score and current OCS dose for participants in BBM.

BS Score		**OCS Titration by current OCS dose**							
Prednisone (mg)	**0**	**5**	**7.5**	**10**	**15**	**20**	**25**	**30**	**37.5**
Dexamethasone (mg)	**0**	**0.75**	**1.25**	**1.5**	**2.25**	**3.0**	**3.75**	**4.5**	**5.75**
2	+ 7.5mg/day OCS (or equivalent)	Increase to 7.5mg/day OCS (or equivalent)	Increase to 10mg/day OCS (or equivalent)	Increase to 15mg/day OCS (or equivalent)	Increase to 20mg/day OCS (or equivalent)	Increase to 25mg/day OCS (or equivalent)	Increase to 30mg/day OCS (or equivalent)	Increase to 37.5mg/day OCS (or equivalent)	Increase to 50mg/day OCS (or equivalent)
1	-	-	-	-	-	-	-	-	-
0	No change, consider ICS reduction	Discontinue OCS	Reduce to 5mg/day OCS	Reduce to 7.5mg/day OCS	Reduce to 10mg/day OCS	Reduce to 15mg/day OCS	Reduce to 20mg/day OCS	Reduce to 25mg/day OCS	Reduce to 30mg/day OCS

Supplemental Figure 1: CONSORT Flow Diagram of enrolment for Markers of Inflammation in the Management Of Severe Asthma: A randomised controlled trial of biomarker based titration of oral corticosteroids study.

Supplemental Figure 2: Markers of inflammation (PBE (Supplemental Figure 2A) and FeNO (Supplemental Figure 2B)) over the course of the study for the biomarker based management (BBM) and standard best practice (SBP) groups. Sputum eosinophil counts are presented at enrolment and the final visit of the study. (Figure 2C)

Supplemental Figure 3: PBE (Supplemental Figure 3A) and FeNO (Supplemental Figure 3B) in participants on mepolizumab over the course of the study in BBM and SBP.

Supplemental Figure 4: OCS dose (mg/day) administered over the study period in BBM and SBP groups.