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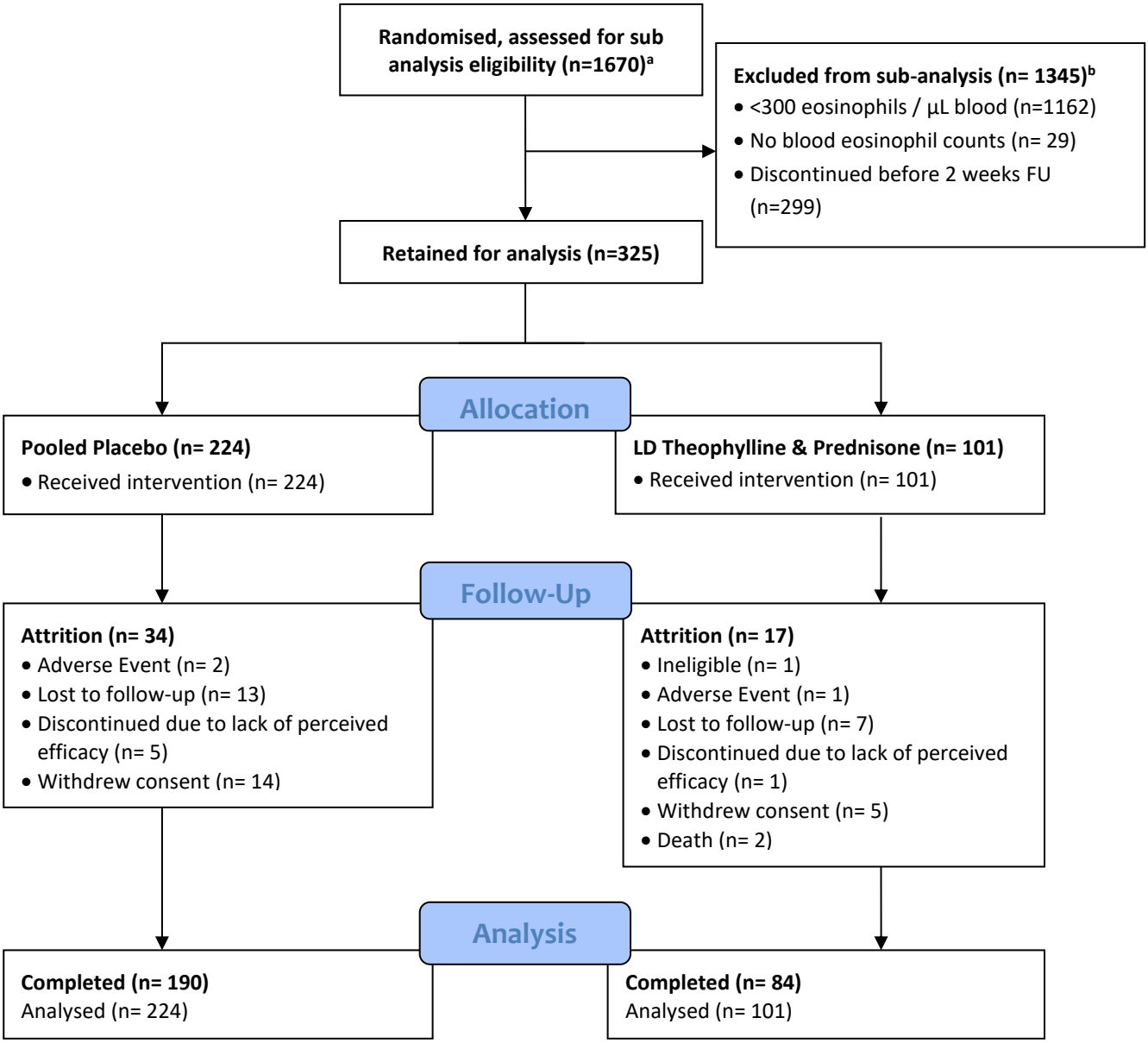
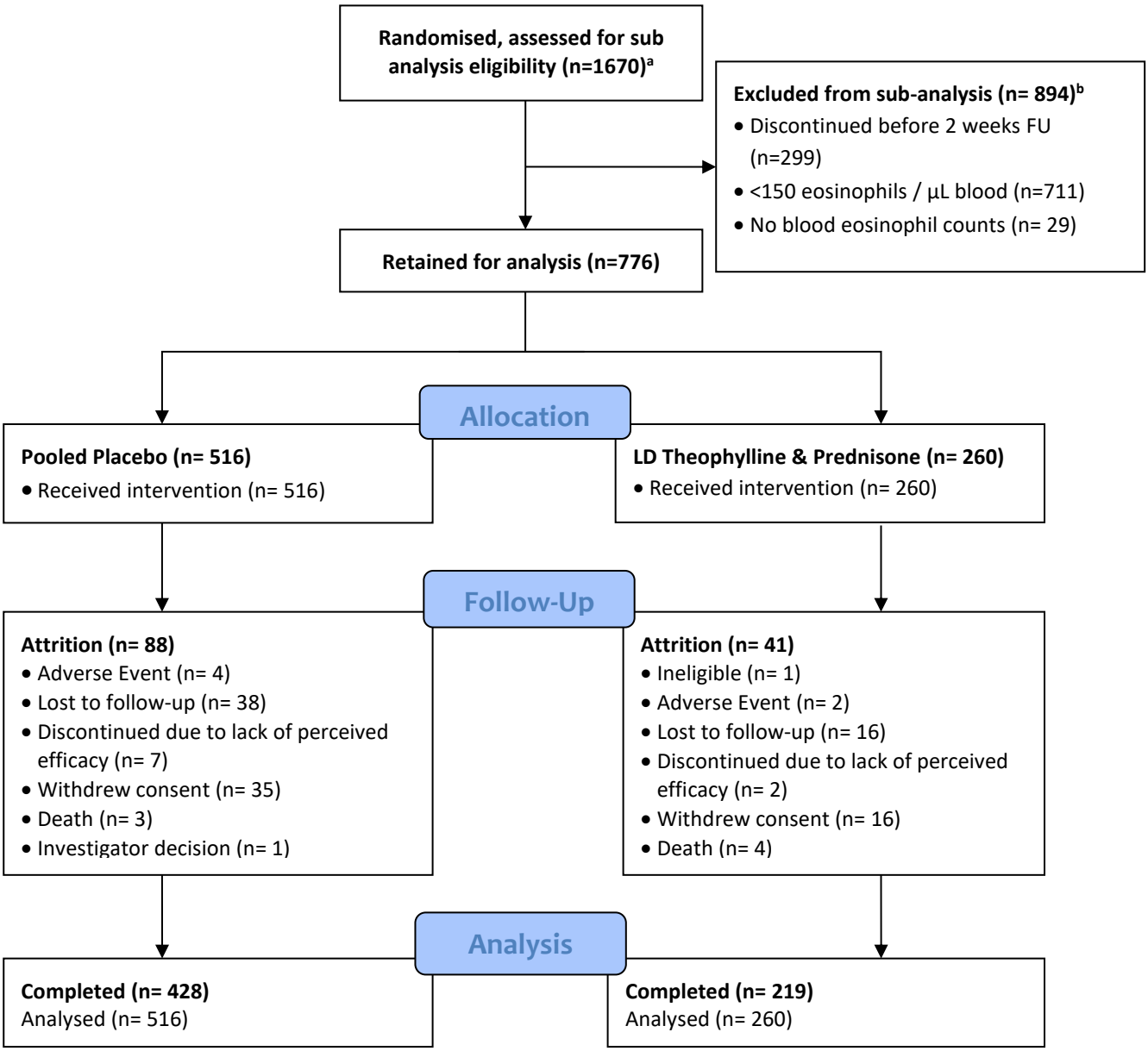


[a] of all participants originally randomized into the trial

[b] participants may have been excluded due to violating more than one of the pre-specified secondary analysis inclusion criteria

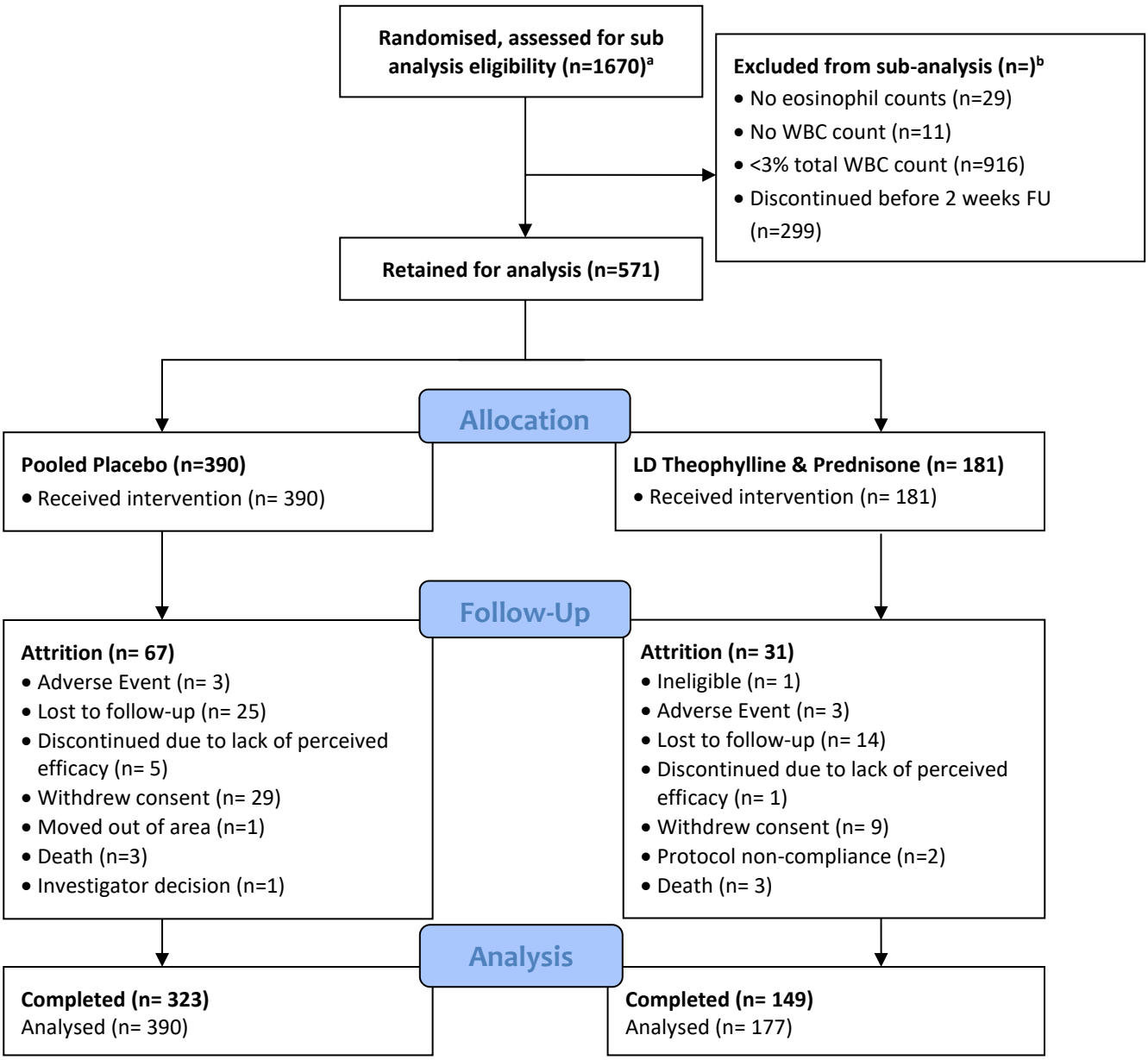
Figure S1A: consort diagram for eligible participant flow from randomisation, assessment of patient post-hoc analysis to study completion for participants with a blood eosinophil count ≥300 cells/µL blood.



[a] of all participants originally randomized into the trial

[b] participants may have been excluded due to violating more than one of the pre-specified secondary analysis inclusion criteria

Figure S1B: consort diagram for eligible participant flow from randomisation, assessment of patient post-hoc analysis to study completion for participants with a blood eosinophil count ≥150 cells/µL blood.



[a] of all participants originally randomized into the trial

[b] participants may have been excluded due to violating more than one of the pre-specified secondary analysis inclusion criteria

Figure S1C: consort diagram for eligible participant flow from randomisation, assessment of patient post-hoc analysis to study completion for participants with a blood eosinophil count ≥3% of the total white blood cell count.

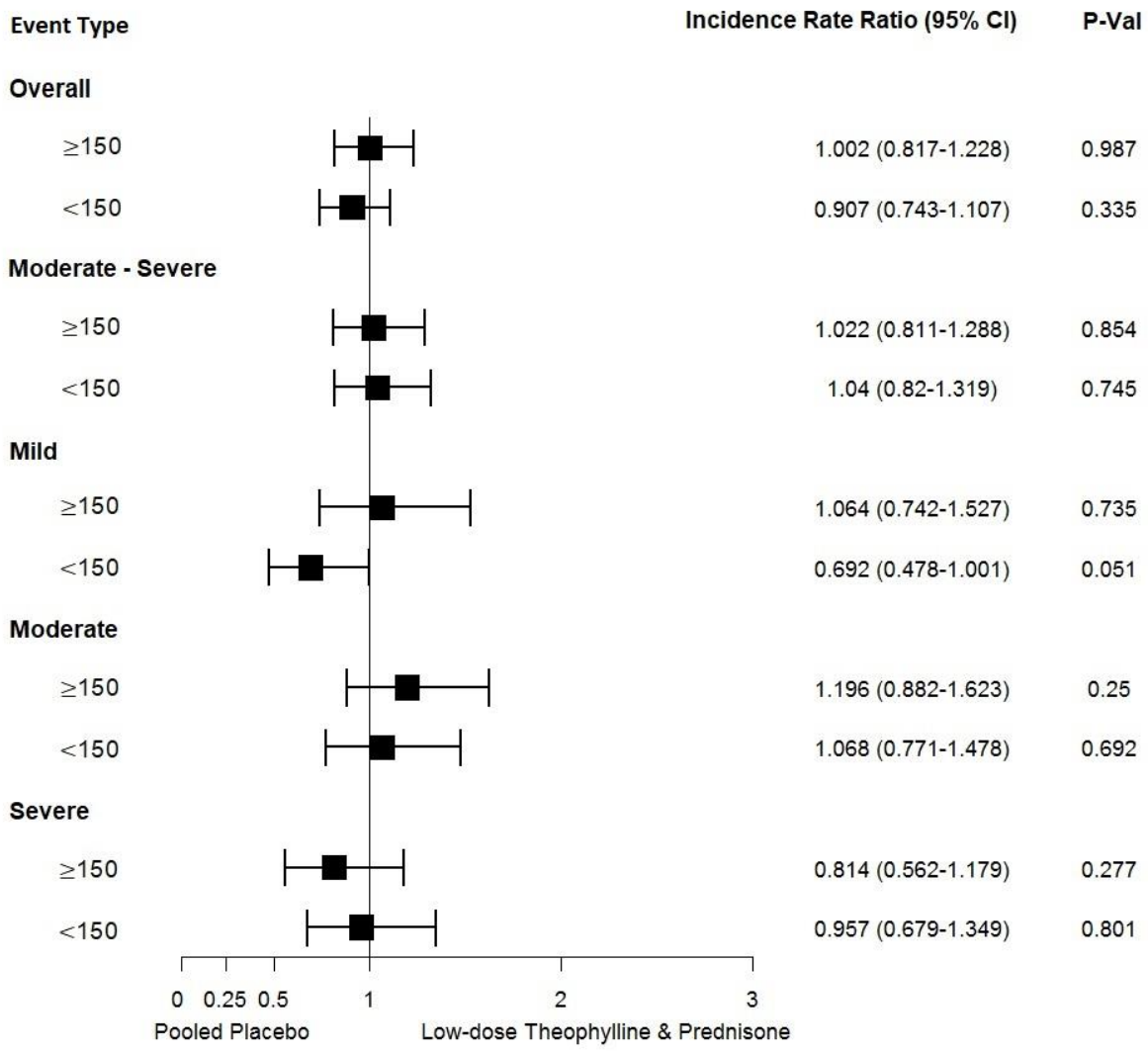


Figure S2A: Incidence Rate Ratios (95% CI) of acute exacerbations of chronic obstructive pulmonary disease between Prednisone & Theophylline and Pooled Placebo study arms in participants with blood eosinophil counts ≥150 cells/µL, derived from a multi-level mixed effects model

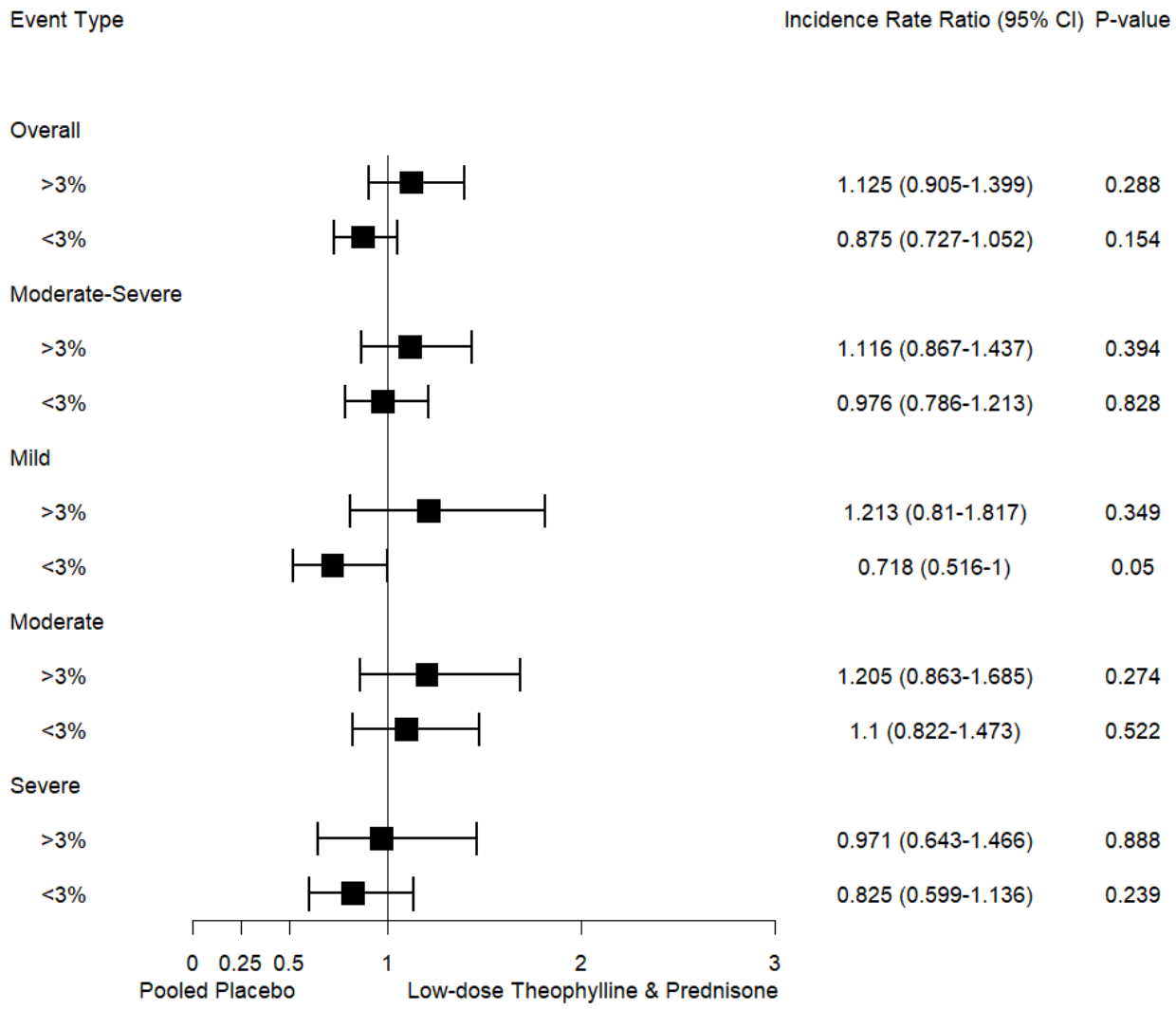


Figure S2B: Incidence Rate Ratios (95% CI) of acute exacerbations of chronic obstructive pulmonary disease between Prednisone & Theophylline and Pooled Placebo study arms in participants with blood blood eosinophil counts ≥3% total white blood cell count, derived from a multi-level mixed effects model

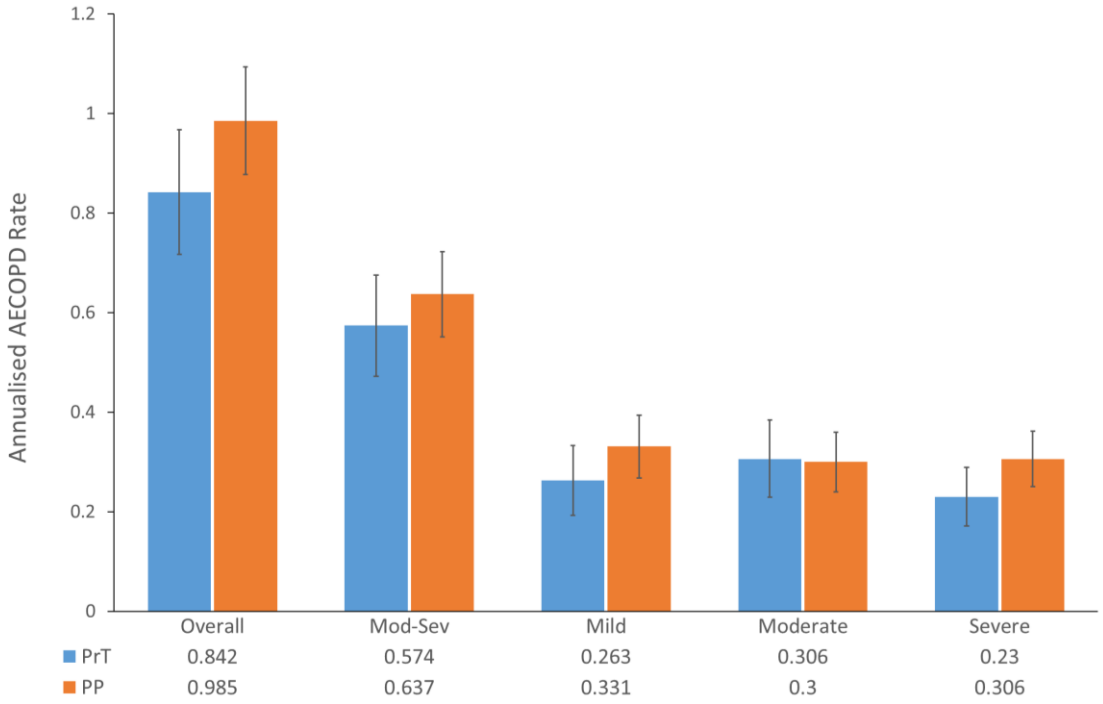


Figure S3A: Adjusted annualised AECOPD rates, stratified by severity, for patients with blood eosinophil counts <300 cells/µL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

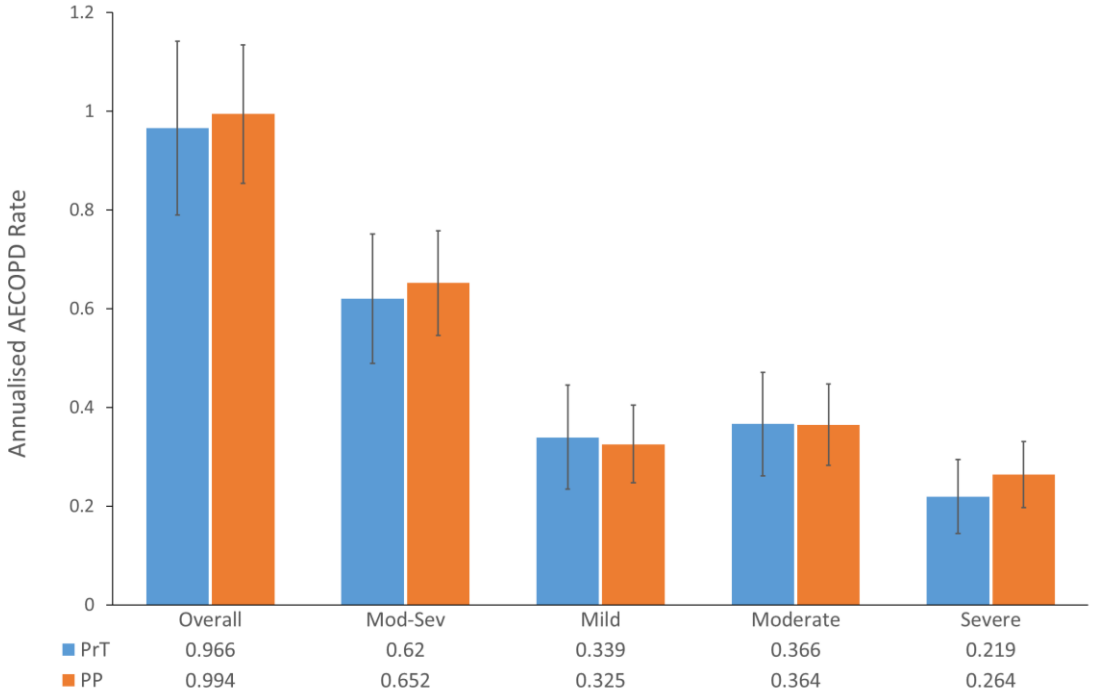


Figure S3B: Adjusted annualised AECOPD rates, stratified by severity, for patients with blood eosinophil counts ≥150x10 cells/µL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

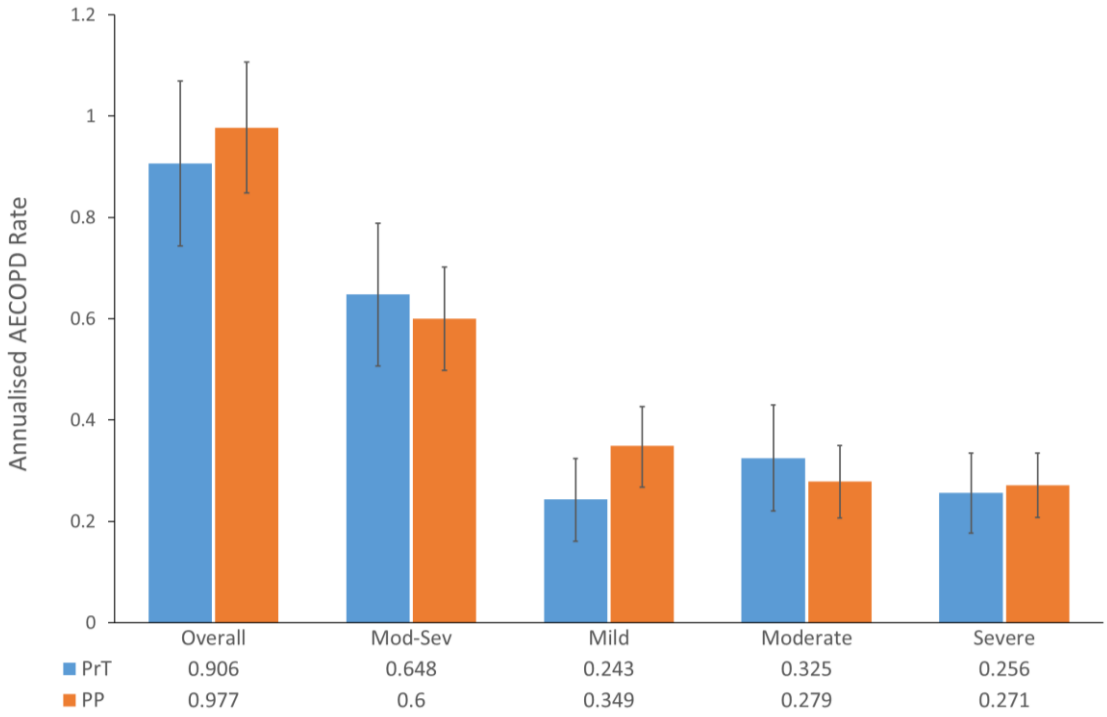


Figure S3C: Adjusted annualised AECOPD rates, stratified by severity, for patients with blood eosinophil counts <150x10 cells/µL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

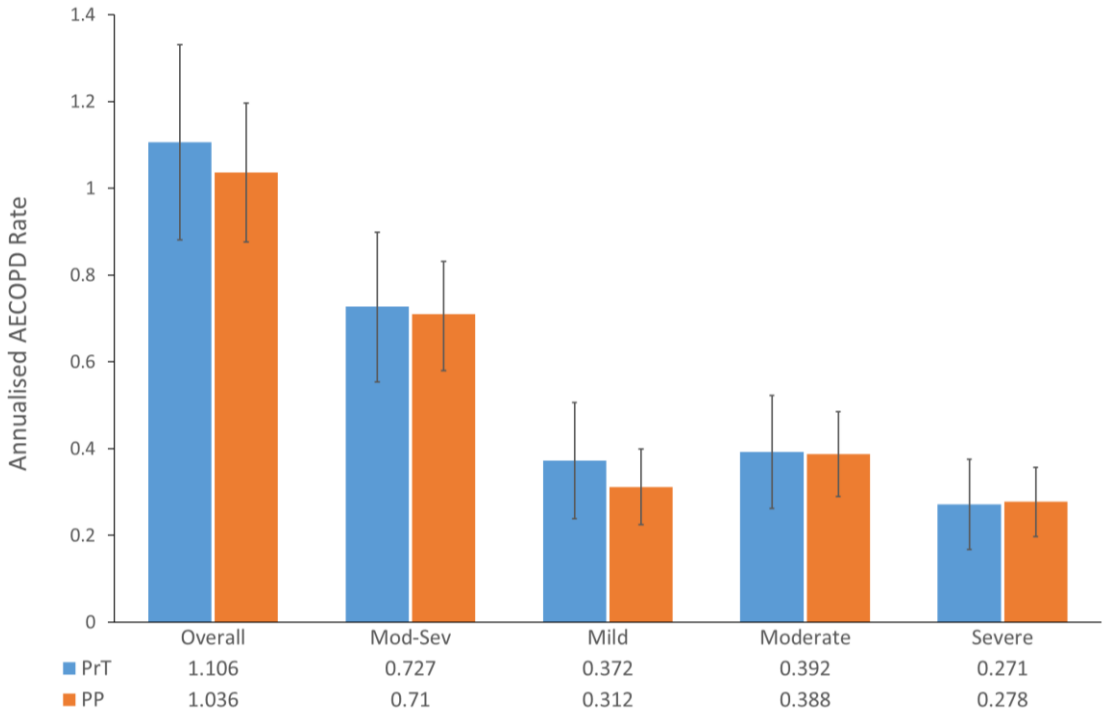
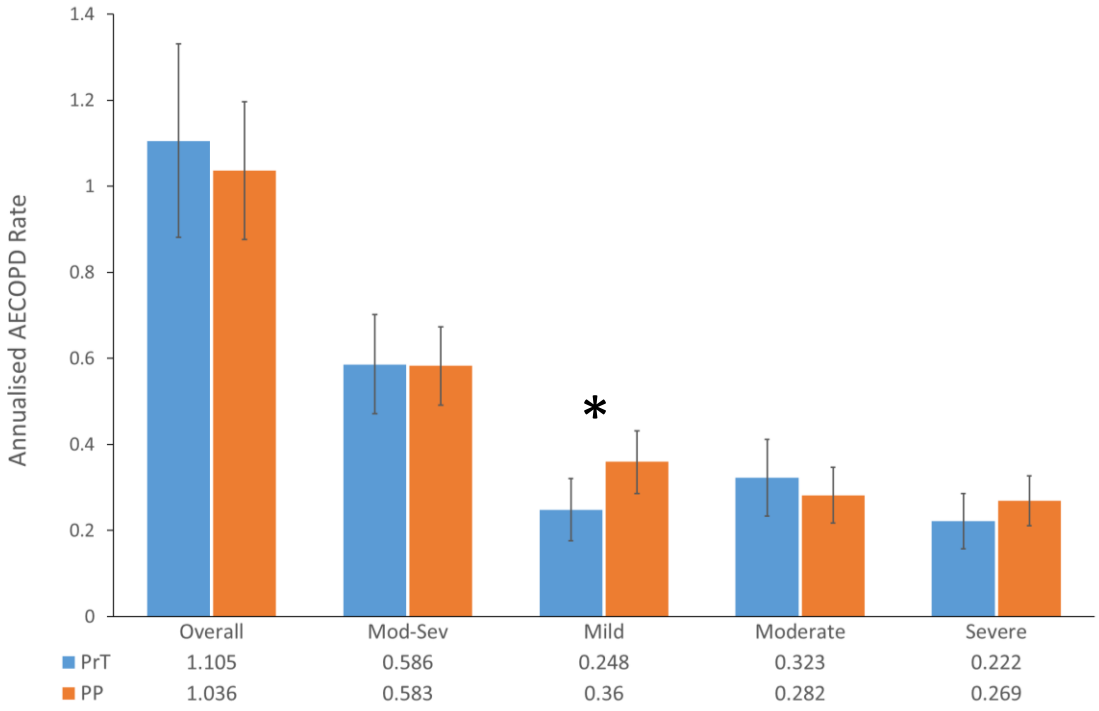


Figure S3D: Adjusted annualised AECOPD rates, stratified by severity, for patients with blood eosinophil counts ≥3% of the total white blood cell count, between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



* p<0.05

Figure S3E: Adjusted annualised AECOPD rates, stratified by severity, for patients with blood eosinophil counts <3% of the total white blood cell count, between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

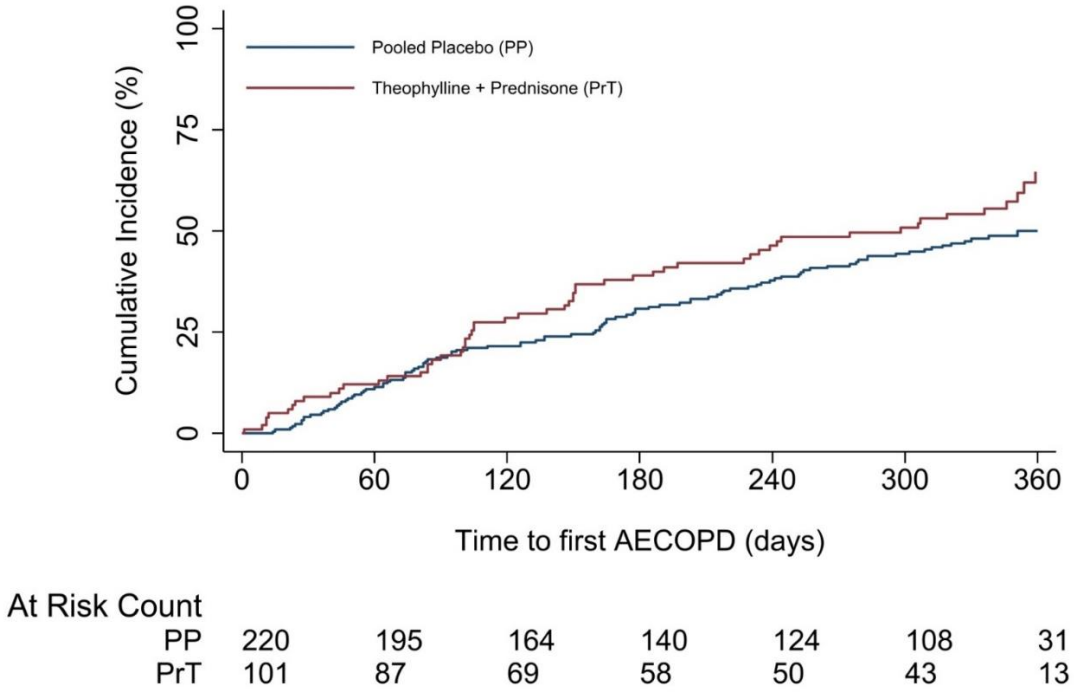


Figure S4A: Time to first acute exacerbation of chronic obstructive pulmonary disease (AECOPD) of any severity in participants with blood eosinophil counts ≥300 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

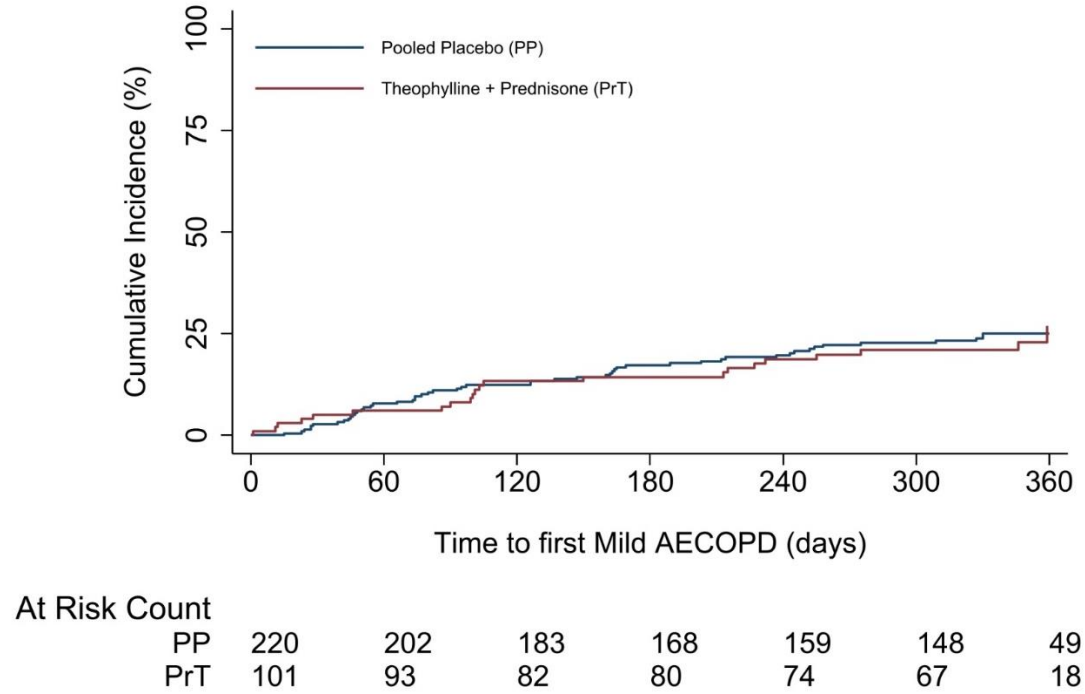


Figure S4B: Time to first mild acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥300 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

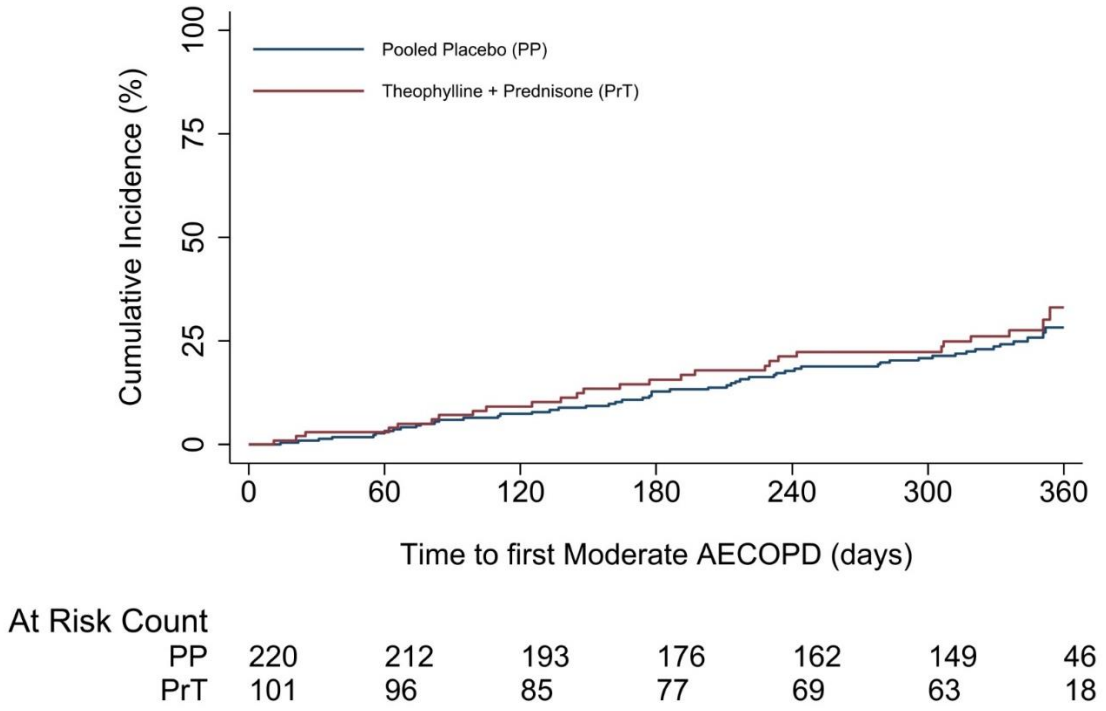


Figure S4C: Time to first moderate acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥300 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

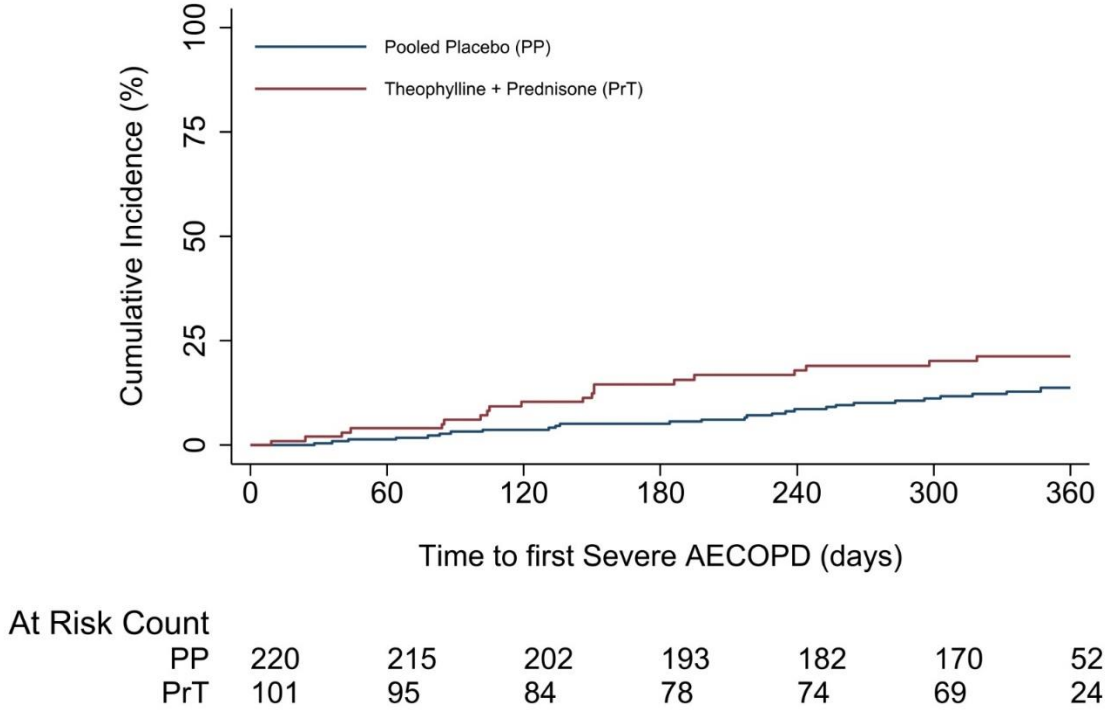
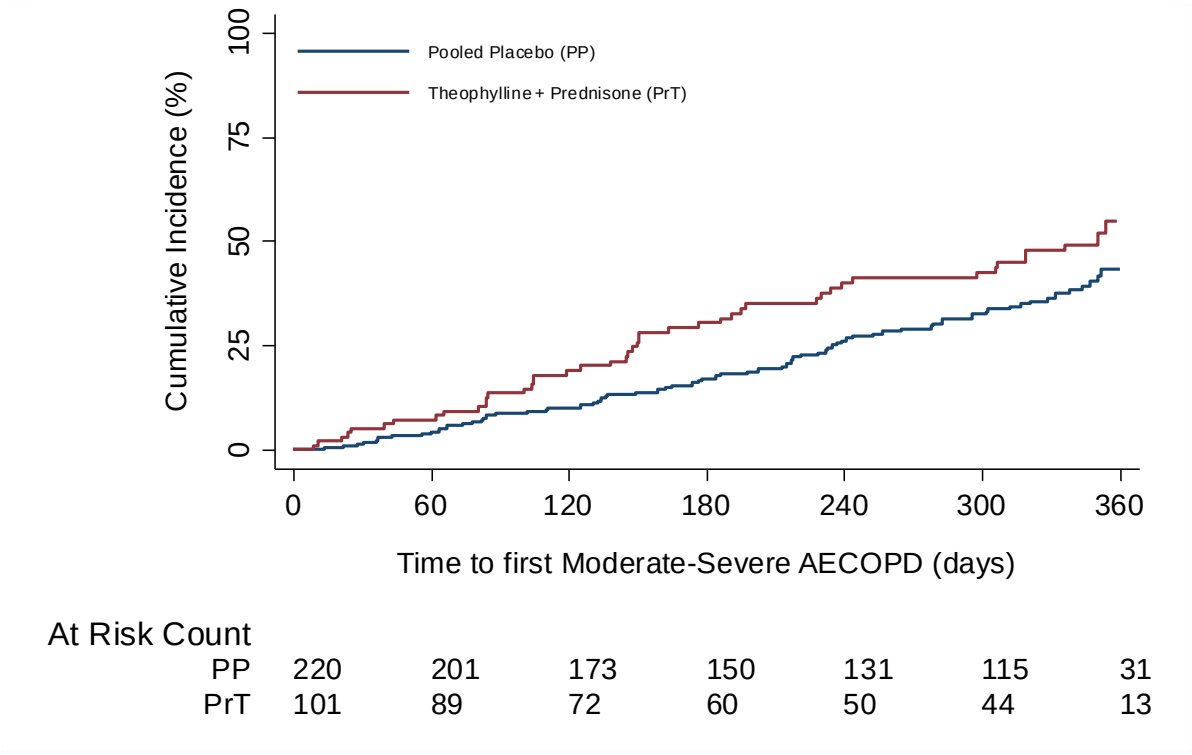


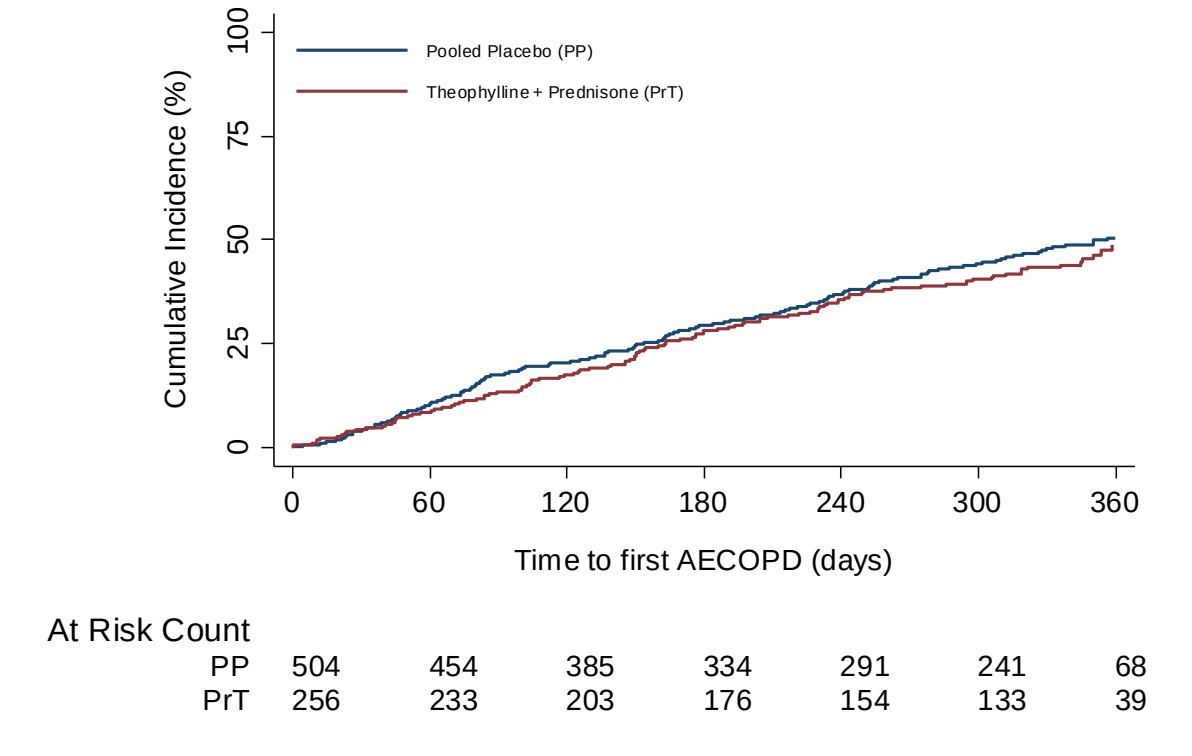
Figure S4D: Time to first severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥300 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



At Risk Count

PP	220	201	173	150	131	115	31
PrT	101	89	72	60	50	44	13

Figure S5A: Time to first moderate-severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥150 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



At Risk Count

PP	504	454	385	334	291	241	68
PrT	256	233	203	176	154	133	39

Figure S5B: Time to first acute exacerbation of chronic obstructive pulmonary disease (AECOPD) of any severity in participants with blood eosinophil counts ≥150 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

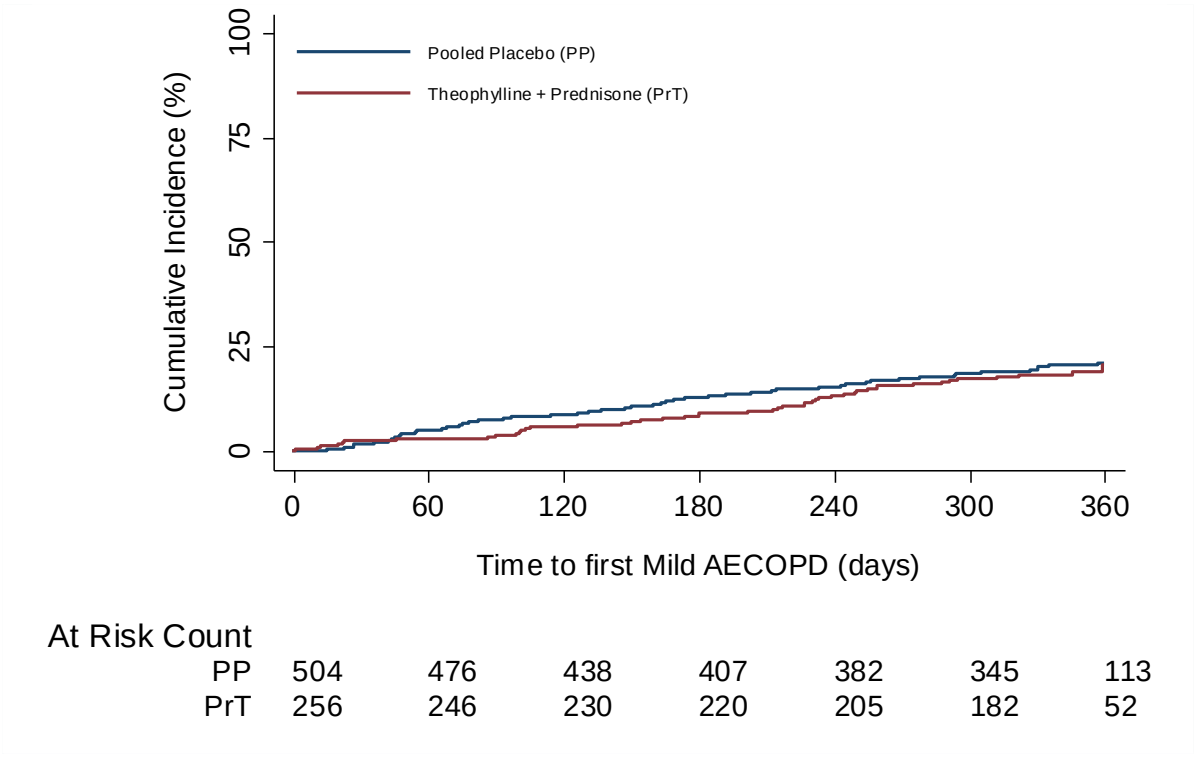


Figure S5C: Time to first mild acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥150 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

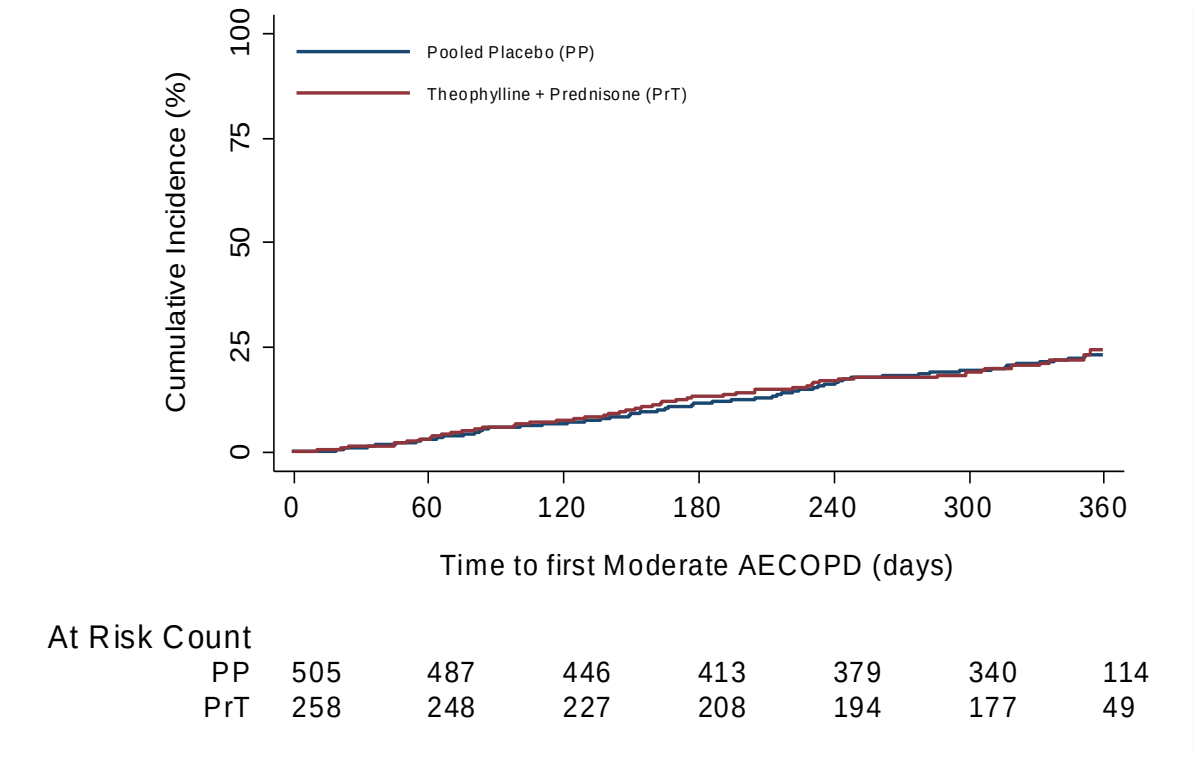


Figure S5D: Time to first moderate acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥150 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.

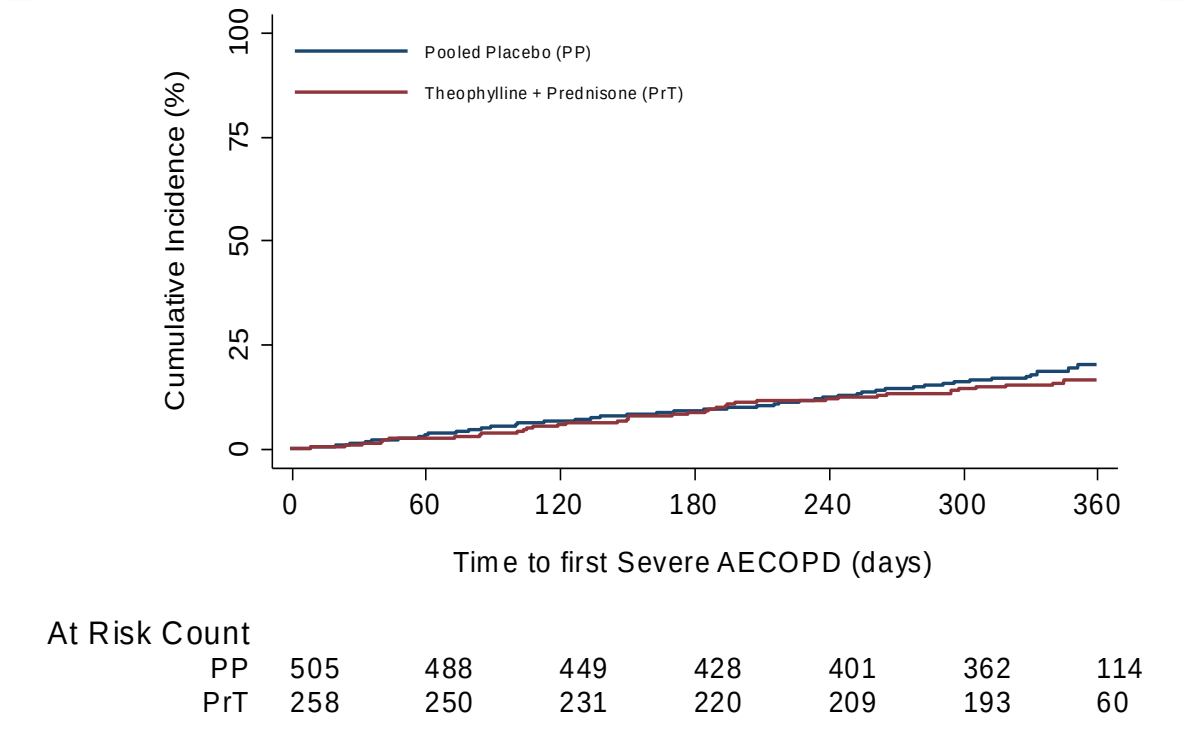
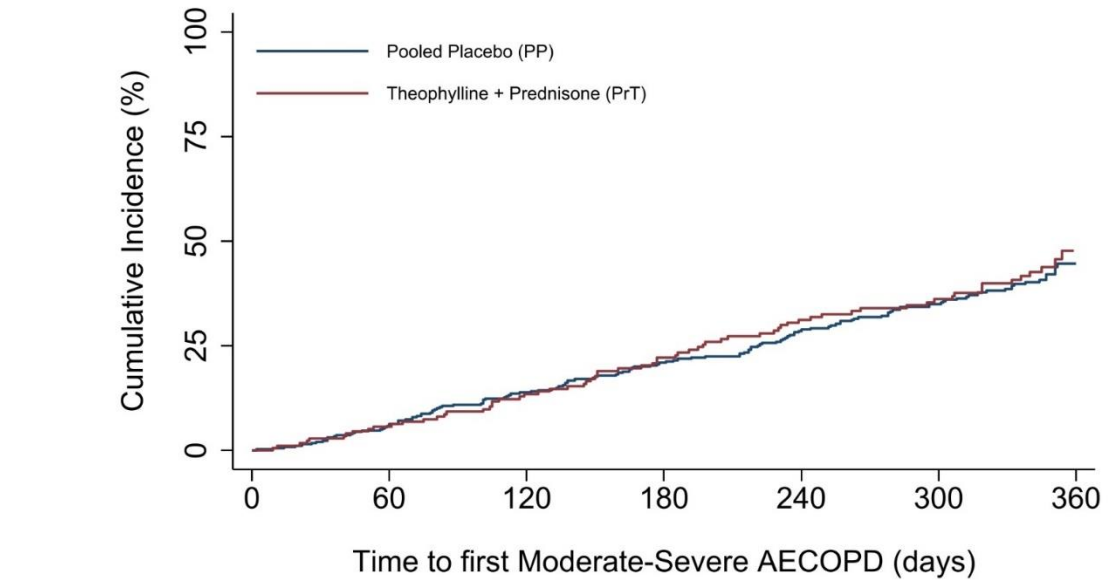


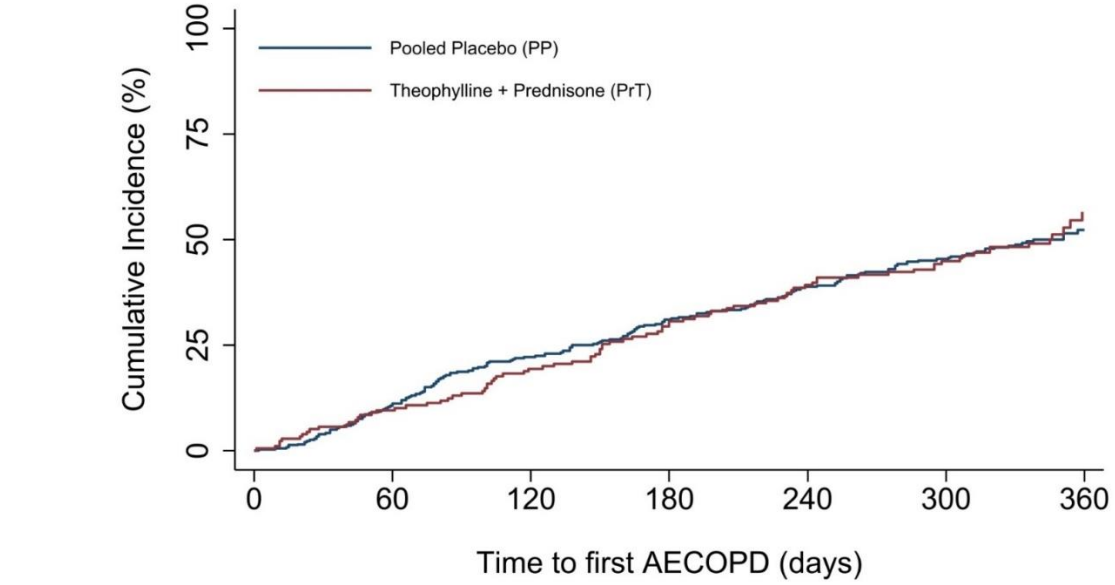
Figure S5E: Time to first severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥150 cells/μL between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



At Risk Count

PP	386	351	297	259	221	185	52
PrT	179	163	142	122	103	87	22

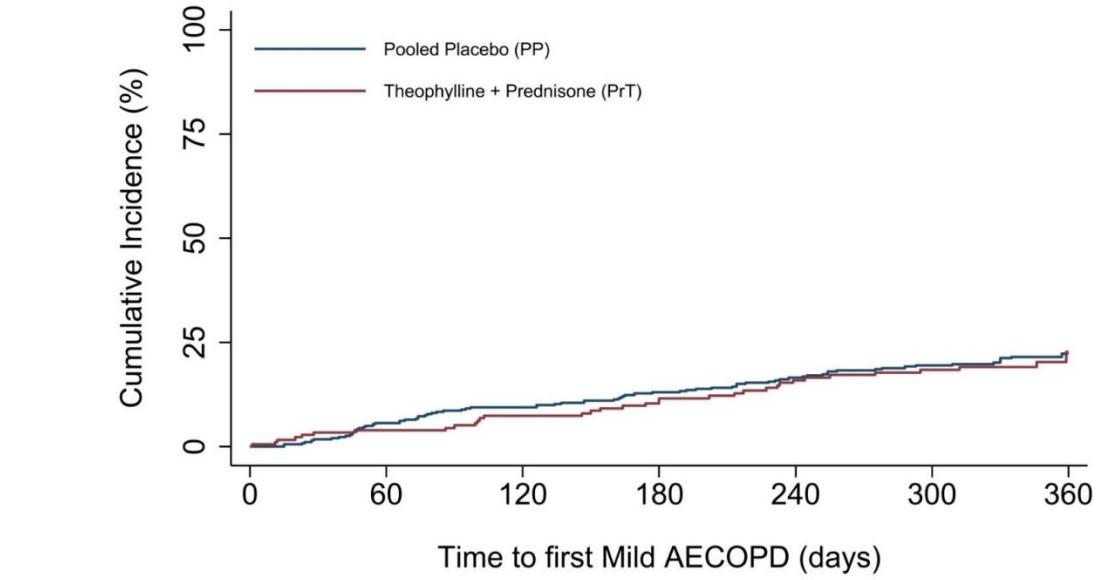
Figure S6A: Time to first moderate-severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥3% total white blood cell count between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



At Risk Count

PP	386	344	284	246	211	177	52
PrT	179	160	138	117	99	84	22

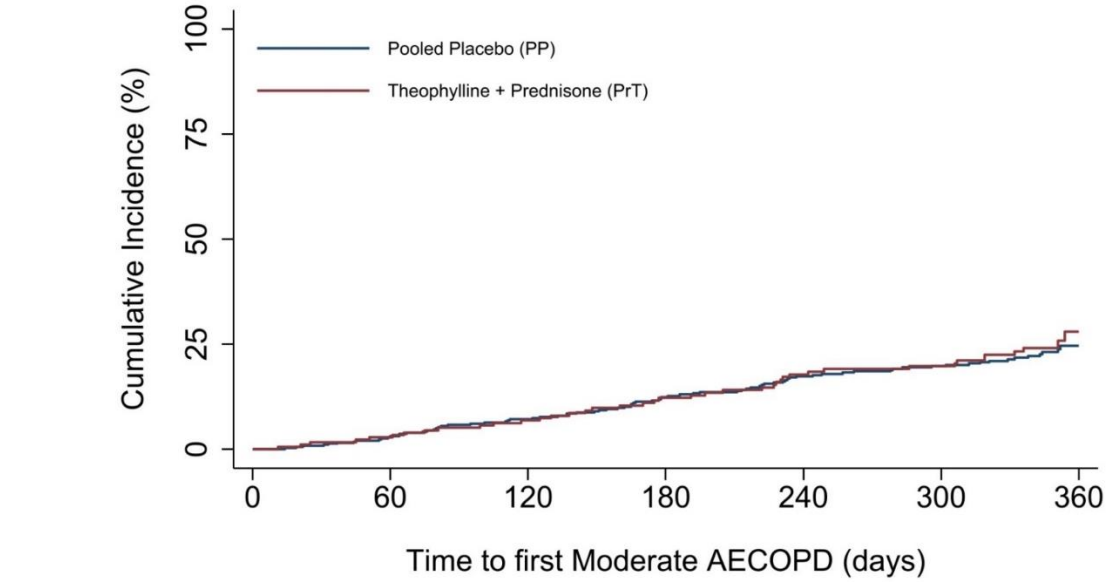
Figure S6B: Time to first acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥3% total white blood cell count between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



At Risk Count

PP	386	362	330	308	284	258	87
PrT	179	170	158	148	136	122	32

Figure S6C: Time to first mild acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥3% total white blood cell count between Prednisone & Theophylline (PrT) and Pooled Placebo (PP) treatment groups.



At Risk Count

PP	386	372	337	309	281	255	86
PrT	180	173	158	143	130	118	29

Figure S6D: Time to first moderate acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥3% total white blood cell count

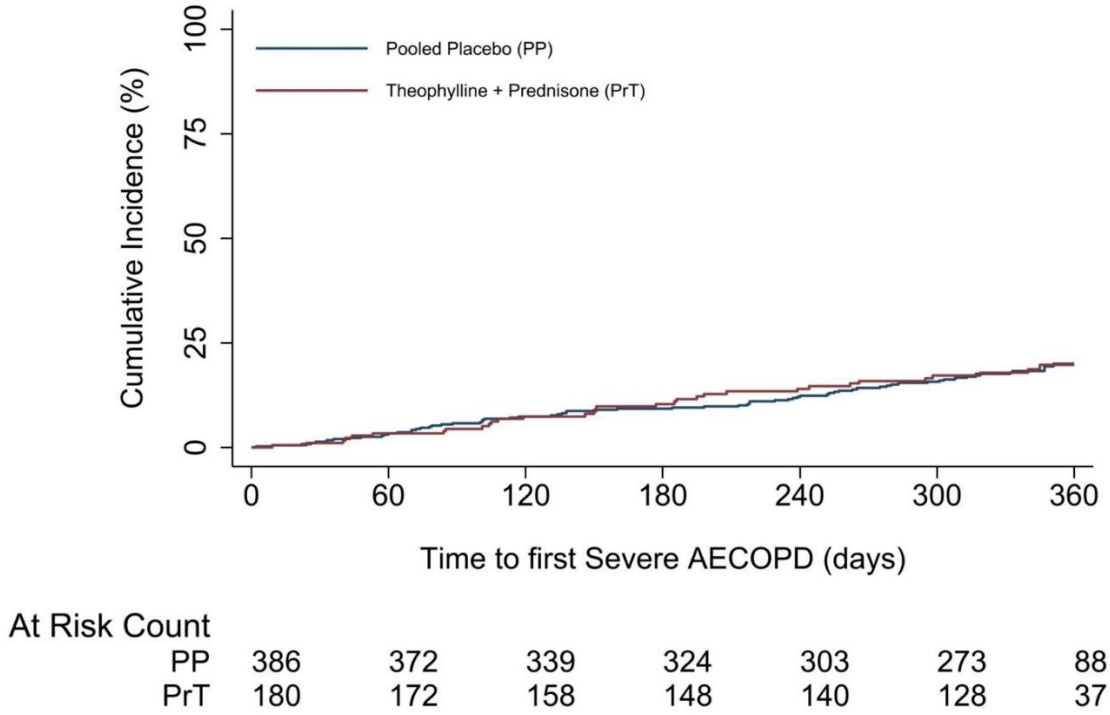


Figure S6E: Time to first severe acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in participants with blood eosinophil counts ≥3% total white blood cell count

Table S1A: Association of Pooled Placebo (PP) and Prednisone and theophylline (PrT) study groups with secondary outcomes at study completion in participants (n=638) with blood eosinophil counts ≥150 cells/µL

	Pooled Placebo (n=428)	Prednisone & theophylline (n=220)	Coefficient	P-Val
CAT Mean[A] Score Change				
	-3.18 (-4.51 – -1.85)	-3.19 (-4.60 – -1.78)	-0.01 (-0.93 – 0.91)	0.984
SGRQ Mean Score Change				
Total	-8.370 (-12.099 – -4.640)	-10.388 (-14.467 – -6.309)	-2.019 (-5.255 – 1.218)	0.222
Symptom	-8.005 (-11.629 – -4.381)	-8.459 (-12.694 – -4.224)	-0.454 (-4.558 – 3.650)	0.828
Activity	-6.325 (-9.515 – -3.135)	-6.526 (-10.167 – -2.885)	-0.201 (-3.504 – 3.101)	0.905
Impact	-6.909 (-10.953 – -2.866)	-9.914 (-13.357 – -4.472)	-2.005 (-5.545 – 1.535)	0.267
Spirometry Mean Change				
FEV1 (L)	-0.01 (-0.04 – 0.02)	-0.003 (-0.04 – 0.03)	0.010 (-0.03 – 0.05)	0.622
FEV1 (%Predicted)[B]	-0.30 (-2.36 – 1.76)	-1.27 (-3.86 – 1.32)	-0.96 (-3.70 – 1.77)	0.490
FVC (L)	-0.06 (-0.13 – 0.02)	-0.02 (-0.10 – 0.07)	0.04 (-0.03 – 0.12)	0.276
FVC (%Predicted)	-1.65 (-4.14 – 0.83)	0.21 (-2.56 – 2.98)	1.86 (-0.55 – 4.23)	0.130
FEV1/FVC (%)	-0.013 (-0.043 – 0.017)	-0.003 (-0.040 – 0.033)	-0.18 (-1.58 – 1.21)	0.796

[A] All means derived from marginal means

[B] Percentage point change

Table S1B: Association of Pooled Placebo (PP) and Prednisone and theophylline (PrT) study groups with secondary outcomes at study completion in participants with blood eosinophil counts ≥3% total white blood cell count

	Pooled Placebo (n=347)	Prednisone & theophylline (n=163)	Coefficient	P-Val
CAT Mean[A] Score Change				
	-3.21 (-4.59 – -1.83)	-3.15 (-4.67 – -1.62)	0.07 (-1.05 – 1.19)	0.906
SGRQ Mean Score Change				
Total	-8.370 (-12.099 – -4.640)	-10.388 (-14.467 – -6.309)	-2.019 (-5.255 – 1.218)	0.222
Symptom	-8.005 (-11.629 – -4.381)	-8.459 (-12.694 – -4.224)	-0.454 (-4.558 – 3.650)	0.828
Activity	-6.325 (-9.515 – -3.135)	-6.526 (-10.167 – -2.885)	-0.201 (-3.504 – 3.101)	0.905
Impact	-6.909 (-10.953 – -2.866)	-9.914 (-13.357 – -4.472)	-2.005 (-5.545 – 1.535)	0.267
Spirometry Mean Change				
FEV1 (L)	-0.015 (-0.049 – 0.019)	0.001 (-0.04 – 0.045)	0.02 (-0.03 – 0.05)	0.501
FEV1 (%Predicted)[B]	0.008 (-1.371 – 1.387)	-0.049 (-1.882 – 1.783)	-0.06 (-2.092 – 1.978)	0.956
FVC (L)	-0.040 (-0.120 – 0.040)	-0.005 (-0.10 – 0.07)	0.03 (-0.06 – 0.12)	0.454
FVC (%Predicted)	-1.388 (-4.074 – 1.296)	-0.083 (-3.205 – 3.040)	1.31 (-1.53 – 4.14)	0.367
FEV1/FVC (%)	0.705 (-0.810 – 2.221)	0.782 (-1.023 – 2.586)	0.076 (-1.62 – 1.78)	0.930

[A] All means derived from marginal means

[B] Percentage point change

Table S2A: Comparison of eosinophilic status (<300 cells/μL of blood vs ≥300 cells/μL of blood) and their association with annualised exacerbation rate within the Pooled Placebo (PP) arm (n = for <300; n = for ≥300) of the TASCS trial

Event Type	Incidence Rate Ratio [A]	Confidence Interval (95%)	P-Value
Overall	0.98	0.80 – 1.19	0.817
Moderate-Severe	0.92	0.73 – 1.17	0.506
Mild	1.14	0.82 – 1.60	0.438
Moderate	1.08	0.80 – 1.46	0.619
Severe	0.71	0.48 – 1.06	0.091

[A] **<**300 cells/μL group coded as 0 in the eosinophilic status (<300 cells/μL of blood vs ≥300 cells/μL of blood) dummy variable

Table S2B: Comparison of eosinophilic status (<300 cells/μL of blood vs ≥300 cells/μL of blood) and their association with annualised exacerbation rate within the combination Prednisone and Theophylline (PrT) arm of the TASCS trial

Event Type	Incidence Rate Ratio [A]	Confidence Interval (95%)	P-Value
Overall	1.56	1.20 – 2.04	0.001
Moderate-Severe	1.56	1.15 – 2.12	0.005
Mild	1.63	0.98 – 2.72	0.061
Moderate	1.45	0.98 – 2.14	0.061
Severe	1.71	1.02 – 2.88	0.042

[A] **<**300 cells/μL group coded as 0 in the eosinophilic status (<300 cells/μL of blood vs ≥300 cells/μL of blood) dummy variable

Table S3A: Univariate predictor analysis of all baseline participant characteristics and their predictive power for continuous blood eosinophil count

Baseline Variable	Regression Coefficient (95% CI)	Standard Error	t-Value	P-Value
Allocated Prednisone + Theophylline	-0.041 (-0.108 – 0.026)	0.034	-1.20	0.228
From Metropolitan Region	0.054 (-0.009 – 0.118)	0.032	1.68	0.093
Male Sex	0.074 (0.0002 – 0.148)	0.038	1.97	0.049
Age	-0.003 (-0.007 – 0.001	0.002	-1.33	0.182
Body Mass Index	0.005 (-0.004 – 0.014)	0.005	0.99	0.321
Is a current/former smoker	0.042 (-0.029 – 0.114)	0.036	1.16	0.244
Had Biomass Exposure	-0.011 (-0.076 – 0.054)	0.033	-0.33	0.739
Had Dust Exposure	0.027 (-0.056 – 0.110)	0.042	0.64	0.525
Post-BD FEV_1 Value (L) [a,b]	0.088 (0.013 – 0.163)	0.038	2.30	0.022
Post-BD FEV_1 Value (%predicted)	0.018 (-0.003 – 0.039)	0.011	1.70	0.090
Pre-Post FEV_1 change (ml)	0.025 (0.001 – 0.049)	0.012	2.00	0.046
Post-BD FEV_1/FVC Ratio [c]	-0.001 (-0.004 – 0.002)	0.001	-0.60	0.552
Post-BD FVC Value (L)	0.067 (0.025 – 0.109)	0.021	3.13	0.002
Post-BD FVC Value (%predicted)	0.002 (0.001 – 0.004)	0.001	2.65	0.008
Past Asthma Dx	0.020 (-0.110 – 0.149)	0.066	0.30	0.764
Systolic Blood Pressure	0.0001 (-0.002 – 0.002)	0.001	0.11	0.916
Diastolic Blood Pressure	0.002 (-0.002 – 0.005)	0.002	0.99	0.322
Heart Rate	-0.002 (-0.005 – 0.0004)	0.001	-1.70	0.090
Respiration Rate	-0.002 (-0.016 – 0.012)	0.007	-0.32	0.746
mMRC Dyspnoea Score [d]	-0.008 (-0.044 – 0.027)	0.018	-0.47	0.637
CAT Score [e]	0.003 (-0.002 – 0.007)	0.002	1.15	0.25
SGRQ - Total Score [f]	0.001 (-0.001 – 0.003)	0.001	1.22	0.222
SGRQ - Active Score	0.002 (0.0001 – 0.003)	0.001	2.03	0.042
SGRQ - Symptom Score	0.001 (0.00002 – 0.003)	0.001	1.99	0.046
SGRQ - Impact Score	0.0002 (-0.001 – 0.002)	0.001	0.25	0.799
Blood Creatinine	0.002 (0.0001 – 0.004)	0.001	1.86	0.063
Blood Glucose	-0.001 (-0.027 – 0.026)	0.013	-0.04	0.969
Blood ALT level [g]	0.001 (-0.002 – 0.003)	0.001	0.47	0.635
Blood AST [h]	0.003 (-0.0004 – 0.006)	0.002	1.70	0.089
Blood Sodium	-0.001 (-0.013 – 0.010)	0.006	-0.25	0.800
Blood White Blood Cell Count	0.023 (0.019 – 0.026)	0.002	12.93	<0.001
Blood Monocyte Count	0.174 (0.148 – 0.201)	0.014	12.72	<0.001
Blood Lymphocyte Count	0.057 (0.047 – 0.067)	0.005	10.97	<0.001
Blood Neutrophil Count	0.016 (0.010 – 0.021)	0.003	5.97	<0.001
Blood Platelet Count	-0.0001 (-0.001 –0.0003)	0.0002	-0.54	0.588
Blood Haematocrit	0.001 (-0.002 – 0.002)	0.001	0.45	0.656

[a] BD, bronchodilator; [b] FEV1, forced expiratory volume – 1 second; [c] FVC, forced vital capacity; [d] mMRC, modified medical research council; [e] CAT, COPD Assessment Test; [f] SGRQ, St. George's Respiratory Questionnaire; [g] ALT, Alanine transaminase; [h] AST, Aspartate transaminase

Table S3B: Univariate predictor analysis of all baseline participant characteristics and their predictive power for a blood eosinophil count ≥300 cells/μL

Baseline Variable	Regression Coefficient (95% CI)	Standard Error	t-Value	P-Value
Allocated Prednisone + Theophylline	-0.125 (-0.390 – 0.139)	0.135	-0.93	0.353
From Metropolitan Region	0.046 (-0.203 – 0.294)	0.127	0.36	0.719
Male Sex	0.410 (0.098 – 0.721)	0.159	2.58	0.01
Age	-0.010 (-0.025 – 0.006)	0.008	-1.22	0.221
Body Mass Index	0.047 (0.012 – 0.082)	0.018	2.61	0.009
Is a current/former smoker	0.164 (-0.122 – 0.449)	0.146	1.12	0.262
Had Biomass Exposure	-0.231 (-0.489 – 0.027)	0.132	-1.75	0.08
Had Dust Exposure	0.215 (-0.097 – 0.527)	0.159	1.35	0.177
Post-BD FEV_1 Value (L) [a,b]	0.068 (0.018 – 0.119)	0.026	2.66	0.008
Post-BD FEV_1 Value (%predicted)	0.068 (-0.013 – 0.148)	0.041	1.64	0.1
Pre-Post FEV_1 change (ml)	0.095 (0.001 – 0.188)	0.048	1.97	0.048
Post-BD FEV_1/FVC Ratio [c]	-0.007 (-0.019 – 0.004)	0.006	-1.27	0.205
Post-BD FVC Value (L)	0.356 (0.195 – 0.517)	0.082	4.33	<0.001
Post-BD FVC Value (%predicted)	0.002 (0.0005 – 0.003)	0.0006	2.84	0.005
Past Asthma Dx	0.095 (-0.400 – 0.589)	0.252	0.38	0.708
Systolic Blood Pressure	-0.002(-0.009 – 0.006)	0.004	-0.42	0.671
Diastolic Blood Pressure	0.006 (-0.006 – 0.019)	0.006	0.97	0.33
Heart Rate	-0.006 (-0.017 – 0.006)	0.006	-1.00	0.316
Respiration Rate	-0.080 (-0.134 – -0.027)	0.027	-2.93	0.003
mMRC Dyspnoea Score [d]	-0.002 (-0.140 – 0.135)	0.070	-0.03	0.974
CAT Score [e]	0.003 (-0.014 – 0.020)	0.009	0.37	0.709
SGRQ - Total Score [f]	0.0003 (-0.006 – 0.006)	0.003	0.08	0.935
SGRQ - Active Score	0.003 (-0.004 – 0.009)	0.003	0.83	0.405
SGRQ - Symptom Score	-0.001 (-0.006 – 0.004)	0.003	-0.43	0.665
SGRQ - Impact Score	-0.0005(-0.006 0.005)	0.003	-0.18	0.857
Blood Creatinine	0.009 (0.002 – 0.016)	0.004	2.49	0.013
Blood Glucose	-0.011 (-0.122 – 0.101)	0.057	-0.19	0.851
Blood ALT level [g]	-0.003 (-0.01319 – 0.007)	0.005	-0.64	0.519
Blood AST [h]	0.005 (-0.007 – 0.018)	0.006	0.88	0.38
Blood Sodium	-0.009 (-0.053 – 0.036)	0.023	-0.38	0.701
Blood White Blood Cell Count	0.038 (0.020 – 0.055)	0.009	4.22	<0.001
Blood Monocyte Count	0.224 (0.128 – 0.319)	0.049	4.60	<0.001
Blood Lymphocyte Count	0.277 (0.127 – 0.426)	0.076	3.63	<0.001
Blood Neutrophil Count	0.021 (0.004 – 0.039)	0.009	2.39	0.017
Blood Platelet Count	0.002 (-0.0002 – 0.003)	0.0009	1.79	0.073
Blood Haematocrit	0.006 (-0.002 – 0.014)	0.004	1.51	0.13

[a] BD, bronchodilator; [b] FEV1, forced expiratory volume – 1 second; [c] FVC, forced vital capacity; [d] mMRC, modified medical research council; [e] CAT, COPD Assessment Test; [f] SGRQ, St. George's Respiratory Questionnaire; [g] ALT, Alanine transaminase; [h] AST, Aspartate transaminase

Table S3C: Univariate predictor analysis of all baseline participant characteristics and their predictive power for a blood eosinophil count ≥150 cells/µL

Baseline Variable	Regression Coefficient (95% CI)	Standard Error	t-Value	P-Value
Allocated Prednisone + Theophylline	0.027 (-0.189 – 0.243)	0.110	0.24	0.808
From Metropolitan Region	0.205 (-0.001 – 0.410)	0.105	1.95	0.051
Male Sex	0.294 (0.054 – 0.534)	0.123	2.4	0.016
Age	0.0003 (-0.013 – 0.013)	0.007	0.05	0.96
Body Mass Index	0.015 (-0.014 – 0.045)	0.015	1.03	0.305
Is a current/former smoker	0.209 (-0.022 – 0.440)	0.118	1.78	0.076
Had Biomass Exposure	-0.138 (-0.348 – 0.072)	0.107	-1.29	0.198
Had Dust Exposure	0.118 (-0.150 – 0.387)	0.137	0.86	0.388
Post-BD FEV_1 Value (L) [a,b]	0.041 (-0.019 – 0.102)	0.031	1.33	0.182
Post-BD FEV_1 Value (%predicted)	0.010 (-0.058 – 0.078)	0.035	0.29	0.771
Pre-Post FEV_1 change (ml)	0.047 (-0.033 – 0.126)	0.040	1.16	0.247
Post-BD FEV_1/FVC Ratio [c]	-0.004 (-0.013 – 0.005)	0.005	-0.88	0.379
Post-BD FVC Value (L)	0.152 (0.014 – 0.288)	0.070	2.16	0.031
Post-BD FVC Value (%predicted)	0.0004 (-0.001 – 0.002)	0.0007	0.55	0.581
Past Asthma Dx	0.273 (-0.150 – 0.697)	0.216	1.27	0.206
Systolic Blood Pressure	0.002 (-0.004 – 0.009)	0.003	0.75	0.456
Diastolic Blood Pressure	0.009 (-0.002 – 0.019)	0.005	1.65	0.1
Heart Rate	-0.001 (-0.010 – 0.009)	0.005	-0.11	0.915
Respiration Rate	-0.019 (-0.064 – 0.026)	0.023	-0.82	0.415
mMRC Dyspnoea Score [d]	-0.064 (-0.177 – 0.050)	0.058	-1.1	0.272
CAT Score [e]	-0.011 (-0.025 – 0.003)	0.007	-1.56	0.118
SGRQ - Total Score [f]	0.0003 (-0.005 – 0.005)	0.003	0.12	0.901
SGRQ - Active Score	0.0004 (-0.005 – 0.006)	0.003	0.14	0.891
SGRQ - Symptom Score	-0.0012 (-0.005 – 0.003)	0.002	-0.55	0.584
SGRQ - Impact Score	0.0007 (-0.004 –0.005)	0.002	0.30	0.768
Blood Creatinine	0.009 (0.003 – 0.015)	0.003	2.81	0.005
Blood Glucose	0.020 (-0.071 – 0.111)	0.046	0.43	0.667
Blood ALT level [g]	0.001 (-0.007 – 0.008)	0.004	0.13	0.9
Blood AST [h]	0.013 (0.002 – 0.024)	0.006	2.3	0.022
Blood Sodium	-0.017 (-0.054 – 0.019)	0.019	-0.93	0.353
Blood White Blood Cell Count	0.025 (0.006 – 0.043)	0.009	2.61	0.009
Blood Monocyte Count	0.192 (0.079 – 0.305)	0.058	3.34	0.001
Blood Lymphocyte Count	0.337 (0.178 – 0.497)	0.081	4.14	<0.001
Blood Neutrophil Count	0.004 (-0.013 – 0.021)	0.009	0.45	0.652
Blood Platelet Count	0.001 (-0.0004 – 0.003)	0.001	1.42	0.155
Blood Haematocrit	-0.001 (-0.008 – 0.005)	0.003	-0.33	0.744

[a] BD, bronchodilator; [b] FEV1, forced expiratory volume – 1 second; [c] FVC, forced vital capacity; [d] mMRC, modified medical research council; [e] CAT, COPD Assessment Test; [f] SGRQ, St. George's Respiratory Questionnaire; [g] ALT, Alanine transaminase; [h] AST, Aspartate transaminase

Table S3D: Univariate predictor analysis of all baseline participant characteristics and their predictive power for a blood eosinophil percentage ≥3% of the total white blood cell count

Baseline Variable	Regression Coefficient (95% CI)	Standard Error	t-Value	P-Value
Allocated Prednisone + Theophylline	-0.112 (-0.335 – 0.111)	0.114	-0.98	0.325
From Metropolitan Region	0.305 (0.093 – 0.517)	0.108	2.81	0.005
Male Sex	0.347 (0.093 – 0.600)	0.129	2.68	0.007
Age	-0.0002 (-0.014 – 0.013)	0.007	-0.03	0.974
Body Mass Index	-0.011 (-0.041 – 0.019)	0.015	-0.71	0.479
Is a current/former smoker	0.116 (-0.122 – 0.355)	0.122	0.96	0.339
Had Biomass Exposure	-0.110 (-0.326 – 0.106)	0.110	-1.00	0.317
Had Dust Exposure	0.255 (-0.016 – 0.526)	0.138	1.84	0.065
Post-BD FEV_1 Value (L) [a,b]	0.201 (-0.048 – 0.449)	0.127	1.58	0.114
Post-BD FEV_1 Value (%predicted)	0.003 (-0.004 – 0.010)	0.004	0.74	0.462
Pre-Post FEV_1 change (ml)	0.060 (-0.021 – 0.141)	0.041	1.44	0.149
Post-BD FEV_1/FVC Ratio [c]	-0.004 (-0.013 – 0.006)	0.005	-0.73	0.467
Post-BD FVC Value (L)	0.185 (0.045 – 0.324)	0.071	2.60	0.009
Post-BD FVC Value (%predicted)	0.003 (-0.002 – 0.009)	0.003	1.16	0.247
Past Asthma Dx	0.091 (-0.335 – 0.517)	0.217	0.42	0.677
Systolic Blood Pressure	-0.003 (-0.010 – 0.003)	0.003	-1.04	0.297
Diastolic Blood Pressure	-0.0002 (-0.011 – 0.010)	0.005	-0.04	0.969
Heart Rate	-0.012 (-0.022 – -0.003)	0.005	-2.49	0.013
Respiration Rate	-0.033 (-0.079 – 0.014)	0.024	-1.38	0.168
mMRC Dyspnoea Score [d]	-0.044 (-0.161 – 0.073)	0.060	-0.73	0.464
CAT Score [e]	-0.005 (-0.019 – 0.010)	0.007	-0.62	0.534
SGRQ - Total Score [f]	-0.002 (-0.008 – 0.003)	0.003	-0.87	0.384
SGRQ - Active Score	-0.004 (-0.007 – 0.004)	0.003	-0.51	0.612
SGRQ - Symptom Score	-0.003 (-0.007 – 0.002)	0.002	-1.19	0.235
SGRQ - Impact Score	-0.002 (-0.007 – 0.002)	0.002	-1.02	0.308
Blood Creatinine	0.010 (0.004 – 0.016)	0.003	3.10	0.002
Blood Glucose	-0.070 (-0.168 – 0.028)	0.050	-1.40	0.162
Blood ALT level [g]	-0.003 (-0.011 – 0.005)	0.004	-0.68	0.493
Blood AST [h]	0.011 (-0.0003 – 0.021)	0.006	1.91	0.056
Blood Sodium	0.008 (-0.030 – 0.046)	0.019	0.43	0.668
Blood White Blood Cell Count	N/A	N/A	N/A	N/A
Blood Monocyte Count	-0.030 (-0.127 – 0.066)	0.049	-0.62	0.537
Blood Lymphocyte Count	-0.008 (-0.045 – 0.029)	0.019	-0.41	0.678
Blood Neutrophil Count	-0.145 (-0.208 – -0.082)	0.032	-4.53	0.000
Blood Platelet Count	-0.002 (-0.004 – -0.0005)	0.0008	-2.58	0.010
Blood Haematocrit	-0.002 (-0.009 – 0.004)	0.003	-0.68	0.498

[a] BD, bronchodilator; [b] FEV1, forced expiratory volume – 1 second; [c] FVC, forced vital capacity; [d] mMRC, modified medical research council; [e] CAT, COPD Assessment Test; [f] SGRQ, St. George's Respiratory Questionnaire; [g] ALT, Alanine transaminase; [h] AST, Aspartate transaminase

Table S4: The Theophylline and steroids in chronic obstructive pulmonary disease study (TASCS) recruiting sites and principal investigators

Site	Site Principal Investigator
West China Hospital of Sichuan University	Wen Fuqiang
The First Affiliated Hospital of Guangzhou Medical College	Zhong Nanshan
Beijing Chao-yang Hospital, Capital Medical University	Lin Yingxiang
Daping Hospital, 3rd Military Medical University	Cui Shehuai
The Military General Hospital of Chengdu PLA	Xiao Zhenliang
First Hospital of Jilin University	Li Dan
People's Hospital of Henan Province	Ma Lijun
The First Affiliated Hospital of Guangxi Medical University	Zhong Xiaoning
Jiangsu Provincial Hospital of State Organ	Liu Jiannan
The First Affiliated Hospital of Nanchang University	Zhang Wei
The Fouth Hospital of China Medical University	Wang Xiaoge
The First Affiliated Hospital of Baotou Medical College	He Huijie
Hejian Municipal People's Hospital	Du Baoliang
Yutian County Hospital, Hebei Province	Wang Jinchao
The First People’s Hospital of Zunyi	Liu Daishun
Leshan People's Hospital	Wei Maogang
Neijiang First People's Hospital	Zhang Yong
Chengdu Second People's Hospital	Yan Hao
Bazhong Central Hospital	Zhang Shiguo
Affiliated Hospital of North Sichuan Medical College	Chen Shaoping
Third People’s Hospital of Mianyang	Wang Kailv
Chengdu Fifth People's Hospital	Wang Jun
The Nuclear Industry 416 Hospital	Xiong Shuguang
The first people's hospital of Liangshan state	Li Li
Sichuan Mianyang 404 Hospital	Wang Limin
Suining Central Hospital	He Zhengguang
Dazhou Central Hospital	Wang Hongjun
Chinese and Western medicine Hospital of Panzhihua	Hu Qiang
Yuxian People's Hospital	Guo Dongshuang
Pengzhou People's Hospital	Weng Bangqiong
Traditional Chinese Medicine Hospital Affiliated to Luzhou Medical College	Ao Suhua
People’s hospital Changji Hui Autonomous Prefecture, Xinjia	Guo Yang
Chengdu Qingbaijiang People's Hospital	Liu Zehui
Wendeng Municipal hospital	Zhao Jinguo
Dong'e people's hospital, Shan Dong Province	Cui Jiadong
Henan Dancheng County People's Hospital	Yang Yuwang
Jiangyou People’s Hospital	Wang Jun