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Supplementary Table 2. Summary of treatment exposure in patients that received at least one dose of study medication

	Masitinib (N=271)	Placebo (N=133)
Completed initial week-36 period	56.8% (154)	63.2% (84)
Entered blinded extension period	48.0% (130)	52.6% (70)
Treated until database lock	31.0% (84)	32.3% (43)
Duration of overall exposure (months)		
Mean ± SD	13.2 ± 12.01	13.1 ± 9.70
Median	8.8	9.4
Range	0 – 81	0 – 49

Supplementary Table 3. Sensitivity analysis of severe asthma exacerbation rates with cohorts according to annualized cumulative oral corticosteroid (prednisone-equivalent) intake

Cohort	Treatment (n)	Exposure (months)	SAER	Rate ratio [95%CI]	Reduction [a]	P-value
Primary population						
>500 mg/year	Masitinib (161)	13.8	0.34	0.59 [0.39, 0.88]	41%	0.009
	Placebo (82)	14.4	0.55			
>1000 mg/year	Masitinib (120)	13.9	0.26	0.49 [0.29, 0.82]	51%	0.006
	Placebo (66)	15.2	0.53			
>1500 mg/year	Masitinib (89)	14.5	0.19	0.43 [0.21, 0.88]	57%	0.020
	Placebo (52)	15.2	0.42			
Eosinophil (≥150 cell/µL) subgroup						
>500 mg/year	Masitinib (127)	13.4	0.32	0.51 [0.39, 0.88]	49%	0.005
	Placebo (60)	13.9	0.60			
>1000 mg/year	Masitinib (92)	13.3	0.22	0.29 [0.29, 0.82]	71%	<0.001
	Placebo (46)	15.2	0.55			
>1500 mg/year	Masitinib (69)	13.9	0.15	0.28 [0.21, 0.88]	72%	0.003
	Placebo (38)	15.5	0.49			

n: number of patients in analysis. SAER: Severe asthma exacerbation rate (annualized rate adjusted for the overall time on treatment). CI: confidence interval. [a] Reduction in the severe asthma exacerbation rate relative to placebo.

Supplementary Table 4. Sensitivity analysis of annualized severe asthma exacerbation rates, wherein severe exacerbations are defined as an increase in stable maintenance OCS dose of at least 40 mg/day (prednisone-equivalent) for at least 3 days

Cohort	Treatment (n)	Exposure (years)	Annualized rate (events/year)	Rate ratio [95%CI]	Reduction[a]	P-value
Primary population						
Overall treatment	Masitinib (240) Placebo (115)	1.14 1.15	0.22 0.4	0.46 [0.31, 0.68]	54%	0.0001
Week 36	Masitinib Placebo	0.54 0.60	0.32 0.5	0.61 [0.38, 0.96]	39%	0.0332
Week 48	Masitinib Placebo	0.65 0.72	0.29 0.55	0.52 [0.34, 0.81]	48%	0.0033
Week 52	Masitinib Placebo	0.69 0.76	0.28 0.53	0.53 [0.34, 0.81]	47%	0.0036
Week 72	Masitinib Placebo	0.84 0.91	0.25 0.47	0.50 [0.33, 0.77]	50%	0.0013
Week 96	Masitinib Placebo	0.97 1.02	0.23 0.42	0.51 [0.34, 0.78]	49%	0.0015
Eosinophil (≥150 cell/µL) subgroup						
Overall treatment	Masitinib (181) Placebo (87)	1.1 1.12	0.23 0.41	0.52 [0.32, 0.82]	48%	0.0055
Week 36	Masitinib Placebo	0.54 0.6	0.31 0.59	0.56 [0.32, 0.97]	44%	0.0399
Week 48	Masitinib Placebo	0.65 0.73	0.27 0.57	0.47 [0.28, 0.79]	53%	0.0043
Week 52	Masitinib Placebo	0.69 0.76	0.26 0.54	0.48 [0.29, 0.81]	52%	0.0053
Week 72	Masitinib Placebo	0.84 0.9	0.24 0.46	0.52 [0.31, 0.85]	48%	0.0097
Week 96	Masitinib Placebo	0.97 1.0	0.23 0.41	0.53 [0.33, 0.87]	47%	0.0123
Full Analysis Dataset (FAS)						
Overall treatment	Masitinib (269) Placebo (133)	1.1 1.09	0.22 0.38	0.47 [0.32, 0.68]	53%	<0.001
Week 36	Masitinib Placebo	0.54 0.6	0.32 0.5	0.60 [0.38, 0.93]	40%	0.0229
Week 48	Masitinib Placebo	0.65 0.72	0.29 0.5	0.53 [0.35, 0.81]	47%	0.0030
Week 52	Masitinib Placebo	0.68 0.75	0.28 0.48	0.53 [0.35, 0.81]	47%	0.0032
Week 72	Masitinib Placebo	0.82 0.88	0.25 0.43	0.52 [0.35, 0.78]	48%	0.0017
Week 96	Masitinib Placebo	0.94 0.98	0.23 0.39	0.53 [0.36, 0.79]	47%	0.0017

n: number of patients in analysis. CI: confidence interval. [a] Reduction in the severe asthma exacerbation rate relative to placebo. Overall treatment: annualized rate adjusted for the overall time on treatment. OCS: oral corticosteroids.

Supplementary Table 5. Secondary endpoint analysis of moderate/severe asthma exacerbation rate (annualized rate adjusted for the overall time on treatment)

Treatment (n)	Exposure (months)	Annualized rate (events/year)	Rate ratio [95%CI]	Reduction [a]	P-value
Primary analysis population					
Masitinib (240)	13.7	0.48	0.64 [0.48, 0.84]	36%	0.001
Placebo (115)	13.8	0.69			
Eosinophil (≥150 cell/µL) subgroup					
Masitinib (181)	13.2	0.48	0.69 [0.49, 0.95]	31%	0.025
Placebo (87)	13.4	0.71			

n: number of patients in analysis. CI: confidence interval. [a] Reduction in the overall asthma exacerbation rate relative to placebo.

Supplementary Table 6. Most common adverse events for masitinib treatment relative to placebo over the study period (AEs listed had incidence ≥3% in ITT population and relative risk >1.0)

Number (%) of pts with at least 1 event	Masitinib (N = 271)	Placebo (N = 133)	Relative risk [95%CI]
Clinical AE			
Vomiting	16 (5.9)	1 (0.8)	7.9 [1.05, 58.6]
Diarrhea	25 (9.2)	3 (2.3)	4.1 [1.26, 13.3]
Rash maculo-papular	11 (4.1)	2 (1.5)	2.7 [0.61, 12.0]
Abdominal pain upper	11 (4.1)	2 (1.5)	2.7 [0.61, 12.0]
Nausea	25 (9.2)	6 (4.5)	2.0 [0.86, 4.86]
Weight decreased	29 (10.7)	8 (6.0)	1.8 [0.84, 3.78]
Laboratory-related AE			
Blood calcium decreased	15 (5.5)	1 (0.8)	7.4 [0.98, 55.1]
Hemoglobin decreased	20 (7.4)	4 (3.0)	2.5 [0.86, 7.04]
Aspartate aminotransferase increased	33 (12.2)	7 (5.3)	2.3 [1.05, 5.09]
Blood phosphorus decreased	35 (12.9)	9 (6.8)	1.9 [0.95, 3.85]
White blood cell count decreased	11 (4.1)	3 (2.3)	1.8 [0.51, 6.34]
Blood creatinine increased	10 (3.7)	3 (2.3)	1.6 [0.46, 5.85]
Alanine aminotransferase increased	22 (8.1)	7 (5.3)	1.5 [0.68, 3.52]
Blood lactate dehydrogenase increased	21 (7.7)	7 (5.3)	1.5 [0.64, 3.38]
Hematocrit decreased	9 (3.3)	3 (2.3)	1.5 [0.41, 5.35]
Hypoalbuminemia	9 (3.3)	3 (2.3)	1.5 [0.41, 5.35]
Blood urea increased	13 (4.8)	5 (3.8)	1.3 [0.46, 3.50]
Gamma-glutamyl transferase increased	32 (11.8)	13 (9.8)	1.2 [0.66, 2.22]
Lymphocyte count decreased	20 (7.4)	8 (6.0)	1.2 [0.56, 2.71]
Blood cholesterol increased	19 (7.0)	8 (6.0)	1.2 [0.52, 2.59]
Blood albumin increased	11 (4.1)	5 (3.8)	1.1 [0.38, 3.04]
Red blood cell count decreased	14 (5.2)	0 (0.0)	NA

Any given AE can be listed under multiple MedDRA preferred terms. AEs were recorded until 28 days after treatment interruption. N/A: Not applicable

Supplementary Figure 1. Time-series plot of average relative change in peripheral blood eosinophil count from baseline (eosinophil ≥150 cell/µl subgroup) over 36 weeks (measured weekly over first 8 weeks, then every 4 weeks thereafter). Masitinib treatment did not affect eosinophil count in patients with eosinophilic asthma.