ONLINE SUPPLEMENT

Table S1: Comparison of baseline characteristics of the patients who completed the study period vs. those who dropped out.

	completed n=141	**drop-out** n=68		*p-value*
Age (y)	64 ± 7.8	65 ± 8.1		0.47
Male - no. (%)	86 (61%)	44 (64.7%)		0.65
Current Smoking - no.	26 (18%)	12(18%)		0.99
Smoking History - Packyears	50 ± 28	49 ± 35		0.42
COPD grade				
GOLD II GOLD III GOLD IV	36 (26%) 50 (35%) 54 (39%)	19 (28%) 27 (40%) 22 (32%)		0.69
FEV1 (l)	1.2 ± 0.6	1.2 ± 0.6		0.85
FEV1 (% pred)	39.8 ± 18.1	39.5 ± 1.7		0.85
FEV1/VC (%)	45.5 ± 14	45.2 ± 14.7		0.98
6MWT (m)	252 ± 109	244 ± 129		0.49
COPD medication - no. LAMA+LABA+ICS LAMA+LABA LAMA+ICS LAMA LABA+ICS SABA+SAMA	 112 (80%) 10 (7%) 0 (0%) 8 (6%) 9 (6%) 2 (1%)	 54 (80%) 1 (1%) 1 (1%) 8 (12%) 4 (6%) 0 (0%)		 0.99 0.11 0.33 0.16 0.99 0.99
Theophylline	7 (5%)	6 (9%)		0.36
Roflumilast	8 (6%)	3 (4%)		0.99

Overall, there was no clear difference in demographics between patients who completed and patients who dropped out.

Definition of abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative in Obstructive Lung Disease; FEV1, forced expiratory volume in the 1st second; 6MWT, six minutes walk test; LAMA, long acting muscarinic antagonist; LABA, long acting beta-2 agonist; ICS, inhaled corticosteroid, SABA, short acting beta-2 agonist; SAMA, short acting muscarinic antagonist

Table S2: Potential predictors for dropping out (logistic regression with 'dropout' (yes vs. no) as the dependent variable.

	Odds ratio (95% confidence interval)	**p-value (Wald test)**
Simvastatin group (vs placebo)	0.85 (0.25 to 2.85)	0.788
Age (years)	1.00 (0.92 to 1.07)	0.797
Male (vs female	0.29 (0.068 to 1.28)	0.102
Smoker (yes/no)	1.43 (0.29 to 7.02)	0.661
Weight (kg)	1.0 (0.967 to 1.03)	0.876
Theophylline	1.93 (0.093 to 40.1)	0.670
Smoking (log (packyears))	1.31 (0.32 to 5.30)	0.706
COPD		
Grade II	1.00 (-)	reference
Grade III	0.64 (0.13 to 3.19)	0.585
Grade IV	0.10 (0.01 to 0.74)	0.024
Inclusion period	0.6 (0.27 to 1.24)	0.159

For a more detailed analysis of the predictors for dropout see Table S3/S4 and Figure S1

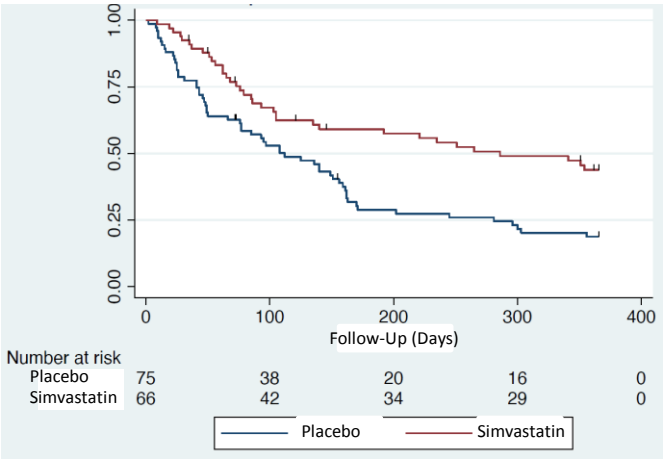
Table S3: Number of patients who dropped out by COPD severity and treatment allocation:

	Simvastatin	**Placebo**	Sum
COPD grade II	**10**	**9**	19
COPD grade III	**16**	**11**	27
COPD grade IV	**13**	**9**	22
Sum	39	29	68

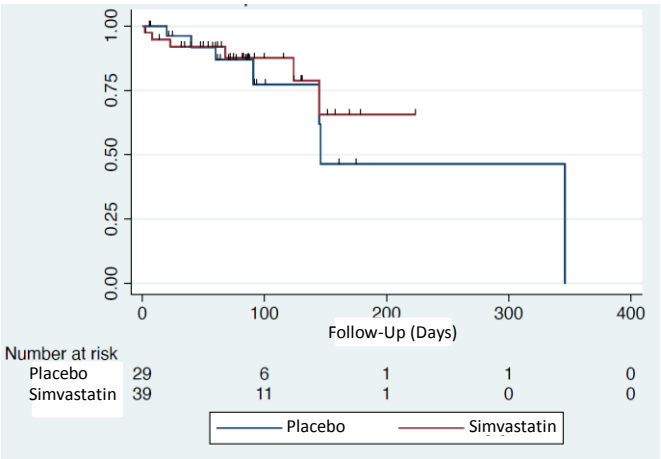
There was no significant interaction between COPD severity and treatment allocation on dropout-status as assessed by the likelihood ratio test (p= 0.3682).

Figure S1 (a and b): Kaplan Meier Plots for time to first exacerbation in participants who did not drop out (a) and participants who dropped out (b).

Participants who did not drop out (a)



Participants who dropped out (b)



The Kaplan Meier plot after removing patients who dropped out remained virtually unchanged compared to the overall Kaplan Meier plot as presented. The plot for the drop-out participants needs to be interpreted with caution due to a potential violation of proportionality and the small subset, but still the patterns of the effect are not conflicting with the overall effect. Moreover, there was no interaction of the effect of simvastatin versus placebo on survivor function by dropout (p= 0.69), which supports our findings that dropout did not explain a large part of our results (Table S4):

Table S4: Comparison of the main effect from all participants and the subset of participants who did not drop out.

	Hazard Ratio (95% confidence interval)	**p-value**
Main effect – all participants	0.506 (0.342 to 0.749)	0.001
Main effect – excluding participants who dropped out	0.503 (0.330 to 0.766)	0.001

Overall, based on the available data dropout is not well explained by a single identifiable factor, there is no major difference between the intention-to-treat and per protocol analysis, and dropouts do not significantly modify the treatment effect, which supports the robustness of our data. Accordingly, based on our measurable and available data it is challenging to show how extreme the selectivity of drop-out would need to be to make these results misleading. However, despite these analyses we cannot fully exclude selection bias as a driver for the present results.