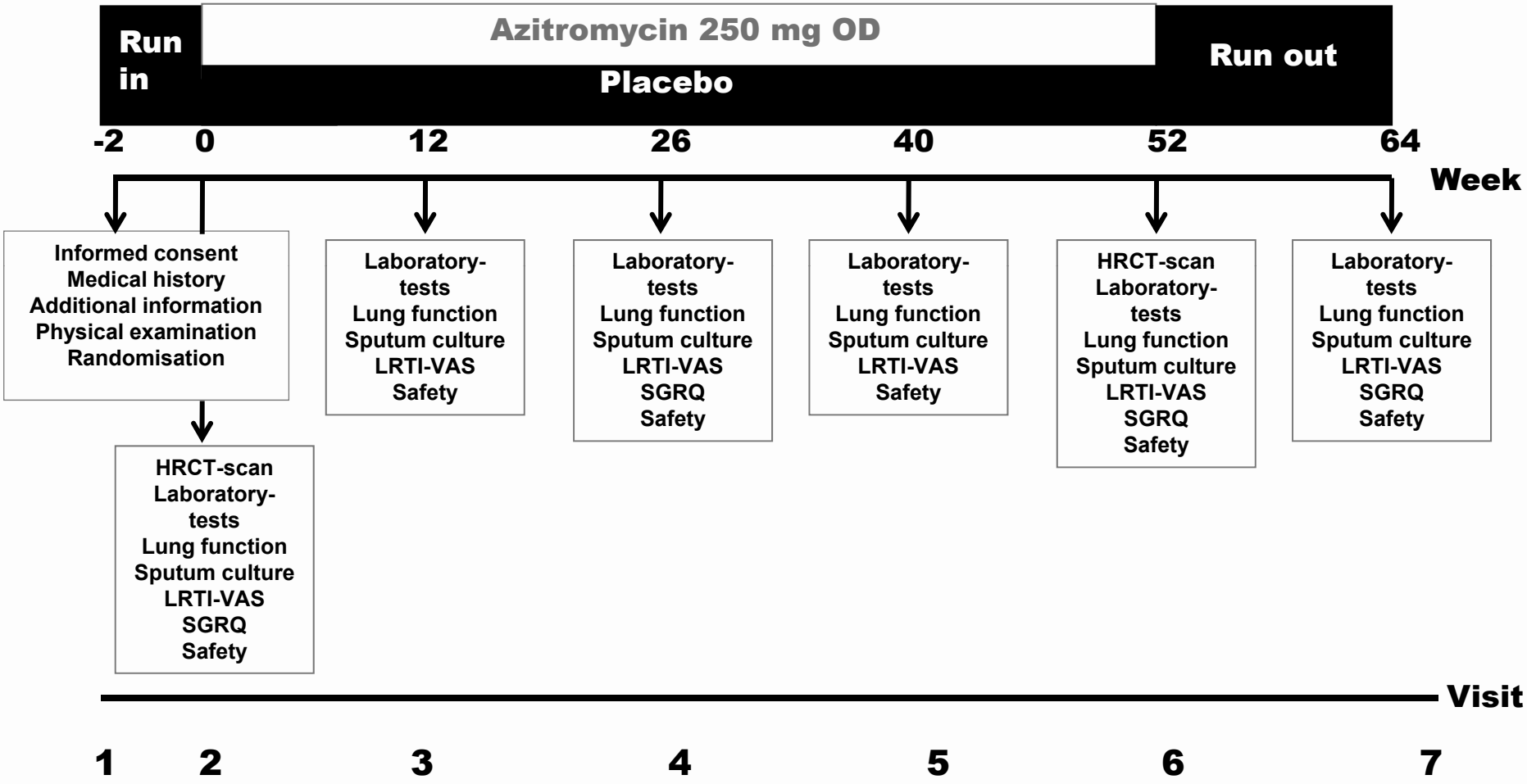
Supplementary Online Content

Altenburg J, de Graaff CS, Stienstra Y, et al. Effect of azithromycin maintenance treatment on infectious exacerbations among patients with non–cystic fibrosis bronchiectasis: the BAT randomized controlled trial. *JAMA*. doi:10.1001/jama.2013.1937

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1: Study schedule:



HRCT: High Resolution Computed Tomography. LRTI-VAS; Lower respiratory Tract Infections- Visual Analogue Scale. SGRQ: St George's Respiratory Questionnaire.

eMethods

Sputum bacteriology:
Gram's stain was performed and sputum quality was assessed. In the Netherlands the washing of sputum, in order to remove the oropharygeal flora, is performed routinely. The presence of >25 polymorphonuclear leukocytes and <10 squamous epithelial cells per low-power field in a Gram-stained sputum was defined as a representative sputum. Representative sputum samples were cultured. Microbiological analysis and susceptibility testing was carried out in accordance with the guidelines of the American Society for Microbiology.

Reference:
Isenberg, H. D. 1992. Clinical microbiology procedures handbook. American Society for Microbiology, Washington, D.C.

LRTI-VAS:
This scale consists of a set of horizontal lines with two anchor points, one at each extreme, each line representing a different symptom. Each symptom is scored from 1 to 10, the subjects being unaware of the numbers. Higher scores indicate more severe symptoms. Five symptom domains are scored: dyspnoea, fatigue, cough, chestpain and sputum colour. Separate scores are calculated for each symptom and a total score is provided, consisting of all symptom scores added up.
Similar weight is assigned to all symptom domains. We used the LRTI-VAS before, to quantify symptoms in 223 patients with acute exacerbations of COPD and in addition to measure clinical outcome in 213 patients with community acquired pneumonia. The LRTI-VAS is currently being validated for use in bronchiectasis by our research group.

Reference:
1. Snijders D, Daniels JM, de Graaff CS, van der Werf TS, Boersma WG. Efficacy of corticosteroids in community-acquired pneumonia: a randomized double-blinded clinical trial. *Am J Respir Crit Care Med* 2010;181:975-982.
Daniels JM, Snijders D, de Graaff CS, Vlaspolder F, Jansen HM, Boersma WG. Antibiotics in addition to systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2010;181:150-157.

eResults

Mixed model analysis on lung function and QoL parameters:

1) Additional information on mixed model on FEV1 %predicted:

The variance of the random intercepts was Var(u_{0j})=615.3, p = < 0.0001, suggesting that the FEV at baseline varied significantly across people. Also, the variance of people's slopes varied significantly Var (u_{1j})=2.1, p = 0.045, suggesting that the change in FEV over time varied significantly across people too. The covariance between the slopes and intercepts was not statistically significant.

FEV1%predicted	b	SE b	95%CI	P
time	-0.10	0.39	-0.91, 0.70	0.80
Treatment *time (placebo = 0)	1.13	0.56	0.17, 2.24	0.047
Treatment	-3.66	5.59	-14.78, 7.46	0.51

2) Additional information on mixed model on FVC %predicted:

The variance of the random intercepts was Var(u_{0j})=492.16, p = < 0.0001, suggesting that the FVC at baseline varied significantly across people. A random slope did not contribute to the model.

FVC % predicted	b	SE b	95%CI	P
Time	-0.30	0.49	-1.27, 0.66	0.535
Treatment *time	1.64	0.68	0.29, 2.99	0.018
Treatment	-6.20	5.05	-16.2, 3.84	0.223

3) Additional information on mixed model on SGRQ:
The variance of the random intercepts was Var(u_{0j})=337.34, p = < 0.0001, suggesting that the SGRQ at baseline varied significantly across people. Also, the variance of people's slopes varied significantly Var (u_{1j})=31.74, p = 0.026, suggesting that the change in SGRQ over time varied significantly across people too. The covariance between the slopes and intercepts was not statistically significant.

SGRQ	b	SE b	95%CI	P
Time	-2.02	1.47	-4.94, 0.91	0.174
Treatment *time	-4.03	1.99	-7.99, -0.067	0.046
Treatment	-2.06	4.56	-11.1, 7.01	0.652

Sputum microbiology

Visit 2 (baseline)	No. of pathogens cultured		No. of pathogens tested		No. macrolide resistant (% of total nr tested)			
	Azithro	Placebo	Azithro	Placebo	Azithro	%	Placebo	%
Haemophilus influenzae	13	9	11	8	5	45,5	3	37,5
Streptococcus pneumoniae	4	4	1	4	0		0	
Staphylococcus aureus	4	8	4	8	1	25,0	2	25,0
Moraxella catarrhalis	4	6	3	6	0		1	16,7
Haemophilus parainfluenza	2	3	1	3	1	100,0	2	66,7
Total	**27**	**30**	**20**	**29**	**7**	35,0	**8**	27,6

Visit 3-7 + exacerbations	No. of pathogens cultured		No. of pathogens tested		No. macrolide resistant (% of total nr tested)			
	Azithro	Placebo	Azithro	Placebo	Azithro	%	Placebo	%
Haemophilus influenzae	53	59	38	48	37	97,4	17	35,4
Streptococcus pneumoniae	1	23	1	14	1	100,0	1	7,1
Staphylococcus aureus	14	33	9	25	6	66,7	4	16,0
Moraxella catarrhalis	7	23	9	19	6	66,7	2	10,5
Haemophilus parainfluenza	5	11	3	6	3	100,0	5	83,3
Total	**80**	**149**	**60**	**112**	**53**	88,3	**29**	25,9

Table. Total numbers of pathogens, numbers of pathogens tested for macrolide resistance and numbers of pathogens with proven macrolide resistance for the most frequently encountered pathogens cultured at baseline (visit 2) and during study treatment (visit 3-7 + exacerbations).