SUPPLEMENTARY MATERIAL

(Online-Only Depository)

I Bronchoscopic procedure and processing of specimens

Surveillance bronchoscopy and broncho-alveolar lavage (BAL) was routinely performed at specific time-points after transplantation (at discharge and 3, 6, 12, 18, 24 months post-transplant, later at intervals of one year) or in case of clinically suspected acute allograft rejection, infection or BOS. Transbronchial biopsies (TBB) were routinely performed at discharge and 3 months post-transplant or in case of clinical suspicion of acute allograft rejection, infection or BOS. Clinical indicators leading to bronchoscopy included symptoms such as dyspnea, cough, sputum, fever, chest radiograph infiltrates, or a decrease in FEV_1 (%predicted) of at least 10% or a decrease of at least 10% in peak expiratory flow (PEF) as measured by patient's daily home peak flow measurements. BAL was performed in a subsegmental bronchus of the right middle lobe (for bilateral or right single lung transplant) or lingula (for left single lung transplant) with two 50 mL aliquots of sterile saline at room temperature. After each instillation, BAL fluid was recovered by gentle manual suction and fractions were pooled for analysis. If indicated, subsequent TBB were performed as outlined in the revised guidelines of the International Society for Heart and Lung Transplantation (ISHLT) in right lower lobe (for bilateral or right single lung transplant) or left lower lobe (for left single lung transplant) [7].

Five mL of the BAL fluid was sent for microbiological and virological assessment, whereas the remaining fluid was immediately transported to the lab for further analysis (Uridraw vacuum test tubes, Terumo Europe, Leuven, Belgium), blinded to the patient's clinical status. A cytospin was made with 10^5 cells/mL in a Shandon cytocentrifuge (Techgen, Zellik, Belgium) and stained

with May-Grünwald-Giemsa. Differential cell counts were determined by counting at least 300 cells. For BAL culture, 100 µl of BAL fluid was serially diluted onto five different media (blood, mannitol salt, MacConkey, Haemophilus selective and Sabouraud agar). Other media were used depending on clinical suspicion (e.g. anaerobes, Legionella, mycobacteria, etc.). The presence of one or more bacterial or fungal colonies after 48 hours of incubation was considered significant and cultures were reported in a standardized, semi-quantitative manner (-, +, ++, +++).

TBB specimens were fixed in formalin, embedded into a paraffin block and subsequently 5 µm histological sections were obtained by serial cutting at two levels and immunohistochemical staining (Hematoxylin-Eosin and Gram staining, if indicated additional staining for *cytomegalovirus* (CMV), *Herpes*, *Pneumocystis*, as well as Verhoeff's Elastica, Ziehl-Neelson and/or Grocott staining) according to standard criteria. All TBB specimens were examined by a single pathologist (EKV) skilled in lung transplantation, who was blinded to the patients' clinical status. TBB were graded according to the 1996 ISHLT-guidelines (grade A0-4 with concomitant B0-4)[7] as well as assessed for other interstitial lesions of the pulmonary graft (e.g. bronchiolitis obliterans organising pneumonia, diffuse alveolar damage, interstitial pneumonitis, etc.).

II Assessment of systemic inflammation

Quantitative determination of plasma C-reactive protein (CRP) levels (obtained before bronchoscopy) was routinely performed at the University Hospital Clinical Lab (Tina-quant CRP latex assay, Roche, Mannheim, Germany; sensitivity threshold of 1 mg/L, upper limit of normal 5 mg/L).

III Assessment of CMV status after transplantation

Cytomegalovirus (CMV)-status was assessed by measurement of blood IgM and IgG antibodies pretransplant and by CMV DNA at weekly intervals during hospitalization and thereafter at each outpatient evaluation or hospital admission. CMV DNA was additionally assessed on every BAL sample. Immunohistochemical staining (MO854, Dako, Belgium) was performed on transbronchial biopsies in case of clinical suspicion of CMV infection.

IV Therapeutic regimen

Immunosuppressive treatment consisted of pre-operative administration of azathioprine (2 mg per kilogram of body weight IV; GSK, Belgium), a high dose of methylprednisolone (500 mg IV; Pfizer, UK) during the transplant procedure and an early post-operative conventional immunosuppressive regimen including methylprednisolone (125 mg tid IV for 24 hours and thereafter 0.4 mg per kg per day), induction therapy with rabbit antithymocyte globulin (rATG) for 3 days (3 mg/kg qd IV; Fresenius, Germany) and administration of a calcineurin inhibitor:

cyclosporine A (2 mg per kg per day continuous IV; Novartis, Belgium) or tacrolimus (0.01-0.015 mg per kg per day continuous IV; Astellas, UK;) and a cytostatic agent: azathioprine (1.5 to 2.5 mg per kg qd IV) or mycophenolate mofetil (1 g bid po; Roche, Switzerland). Immunosuppressives were tapered before discharge. After discharge, both groups received conventional triple-drug immunosuppression with methylprednisolone (0.1-0.4 mg per kg per day), a calcineurin inhibitor: cyclosporine A (3-6 mg per kilogram per day) or tacrolimus (0.05-0.3 mg per kilogram per day) and a cytostatic agent: azathioprine (50-150 mg/d) or mycophenolate mofetil (0.5-3 g per day). Drug choice and dosing adjustments were made according to a standardized protocol at the discretion of the treating clinician on the basis of renal function, immunosuppressive trough levels (target levels for cyclosporine A 200-300 ng per mL, for tacrolimus 5-15 ng per mL), spirometry and biopsy results. Acute rejection (grade A2 or higher) was treated by enhanced immune suppression with pulsed corticosteroids (intravenous methylprednisolone at a dose of 500 mg per day for 3 days), tapered to the oral maintenance dose over the next 2 to 3 weeks. Grade A1 acute rejection was treated by augmenting oral steroids (0.6 mg per kilogram per day for 3 days), similarly followed by tapering. Additionally, in case of recurrent acute rejection, conversion from cyclosporine A to tacrolimus or from azathioprine to mycophenolate mofetil was performed based on a case-by-case decision. There was no strict protocol for treatment of isolated grade B rejection, although most patients were treated with corticosteroids similar to the protocol of acute rejection. Patients developing BOS were treated with azithromycin according to the open-label trial protocol and in case of BOS-progression with conversion of immunosuppressives or, less frequently, total lymph node irradiation (0.8 Gy twice weekly for 5 weeks) or retransplantation. None of our patients received photopheresis treatment for BOS.

Infectious prophylaxis consisted of gancyclovir (Roche, Switzerland) or acyclovir (GSK, Belgium) for CMV (dosing, duration and choice depending on donor and receptor CMV-status, ranging from 5 to 15 mg per kilogram per day for 2 weeks to 2 months), nebulised amphotericin B (UCB, Belgium; 5 mg twice daily during hospitalization) for *Aspergillus* and long-term prophylaxis of sulfamethoxazole-trimethoprim (Roche, Switzerland; 800/160 mg twice a week life-long) for *Pneumocystis*. CMV-related disease or pneumonitis was treated with intravenous ganciclovir (Roche, Switzerland; 5 mg per kilogram twice daily for at least two weeks). *Aspergillus* infection was treated with voriconazole (3-4 mg per kg bid IV or 200 mg bid po; Pfizer, UK). Antibiotic treatment for bacterial infection after transplantation was guided using bacteriologic cultures; airway colonization, however, was not treated by antibiotics, except in cystic fibrosis patients pre-operatively colonized with *P. aeruginosa* in whom post-operatively

colistin nebulisation was initiated (1 million units twice daily for 2 to 3 months; Pharma Logistics, Belgium).

For gastroesophageal reflux prophylaxis, all patients received ranitidine (300 mg per day; GSK, Belgium) or a low dose proton pump inhibitor (20 mg omeprazole or equivalent per day) if gastroesophageal reflux disease had been diagnosed before transplantation. If reflux was diagnosed after transplantation by either pH impedance measurement or gastroscopy, ranitidine was switched to a high dose proton pump inhibitor or the dose of the latter was augmented (40 mg omeprazole or equivalent per day). None of the included patients underwent fundoplication surgery after transplantation.

V Supplementary Tables

Table S1: Immunosupressive regimen

	Placebo (n=43)	Azithromycin (n=40)	p-value
Induction therapy with rATG/none, n (%)	39/4 (90.7/9.3)	38/2 (95.0/5.0)	0.68
Trough level CsA at day 1, µg/L	189.6 (±64.9)	173.9 (±59.2)	0.26
At discharge			
Daily dose prednisolone, mg	28.3 (±7.2)	27.1 (±10.1)	0.15
CNI-regimen			
Patients on CSA/FK, n (%)	20/23 (46.5/53.5)	13/27 (32.5/67.5)	0.19
Daily dose CsA, mg	305.6 (±147.8)	356.0 (±136.2)	0.38
Trough level CsA, µg/L	294.3 (±66.0)	286.4 (±94.4)	0.77
Daily dose FK, mg	8.7 (±4.2)	8.9 (±4.2)	0.88
Trough level FK, µg/L	16.4 (±23.7)	12.0 (±3.6)	0.34
Cytostatic regimen			
Patients on AZA/MMF, n (%)	38/1 (88.4/2.3)	35/2 (87.5/5.0)	0.52
Daily dose AZA, mg	75.7 (±25.0)	72.1 (±27.6)	0.57
Daily dose MMF, mg	3000.0 (±0.0)	2000.0 (±0.0)	NA
Trough level MMF, mg/L	0.9 (±0.0)	1.4 (±0.4)	NA
At 3 months			
Daily dose prednisolone, mg	16.0 (±6.1)	16.6 (±4.1)	0.17
CNI-regimen			
Patients on CSA/FK, n (%)	10/32 (23.3/74.4)	8/31 (20.0/77.5)	0.72
Daily dose CsA, mg	270.0 (±97.8)	296.9 (±97.7)	0.57
Trough level CsA, µg/L	288.7 (±91.6)	313.0 (±32.9)	0.49
Daily dose FK, mg	8.0 (±4.5)	7.4 (±3.9)	0.59
Trough level FK, µg/L	12.5 (±3.0)	11.6 (±3.1)	0.23
Cytostatic regimen			
Patients on AZA/MMF, n (%)	31/3 (72.1/7.0)	30/6 (75.0/15.0)	0.33
Daily dose AZA, mg	78.2 (±28.7)	75.0 (±27.9)	0.66
Daily dose MMF, mg	2000.0 (±1000.0)	1750.0 (±612.4)	0.65
Trough level MMF, mg/L	2.8 (±2.2)	1.8 (±1.9)	0.53
At 6 months			
Daily dose prednisolone, mg	9.6 (±5.5)	8.8 (±2.0)	0.17
CNI-regimen			
Patients on CSA/FK, n (%)	7/33 (16.3/76.7)	4/32 (3.2/80.0)	0.43
Daily dose CsA, mg	332.1 (±68.8)	281.3 (±47.3)	0.23
Trough level CsA, µg/L	254.6 (±79.5)	274.5 (±79.0)	0.70
Daily dose FK, mg	7.3 (±4.9)	6.3 (±3.6)	0.35
Trough level FK, µg/L	11.4 (±3.8)	11.4 (±3.0)	0.96
Cytostatic regimen			
Patients on AZA/MMF, n (%)	26/3 (60.5/7.0)	27/5 (67.5/12.5)	0.54

Daily dose AZA, mg	72.1 (±28.6)	70.4 (±28.6)	0.83
Daily dose MMF, mg	1240.0 (±672.9)	1444.0 (±579.4)	0.66
Trough level MMF, mg/L	1.4 (±1.3)	1.7 (±1.1)	0.82
At 1 year			
Daily dose prednisolone, mg	5.9 (±5.2)	6.6 (±10.1)	0.56
CNI-regimen			
Patients on CSA/FK, n (%)	5/25 (11.6/58.1)	1/30 (2.5/75)	0.078
Daily dose CsA, mg	270.0 (±44.7)	275.0 (±0.0)	NA
Trough level CsA, µg/L	184.8 (±32.8)	191.0 (±0.0)	NA
Daily dose FK, mg	5.5 (±3.5)	6.0 (±2.7)	0.54
Trough level FK, µg/L	9.5 (±2.5)	10.2 (±2.7)	0.33
Cytostatic regimen			
Patients on AZA/MMF, n (%)	25/2 (58.1/4.7)	20/4 (50.0/10.0)	0.31
Daily dose AZA, mg	54.0 (±28.6)	65.0 (±32.9)	0.24
Daily dose MMF, mg	1500.0 (±707.1)	1305.0 (±390.0)	0.67
Trough level MMF, mg/L	1.9 (±0.0)	2.9 (±1.3)	0.38
At 1.5 years			
Daily dose prednisolone, mg	4.1(±0.7)	4.0 (±0.9)	0.82
CNI-regimen			
Patients on CSA/FK, n (%)	4/23 (9.3/53.5)	1/29 (2.5/72.5)	0.13
Daily dose CsA, mg	256.3 (±65.8)	225.0 (±0.0)	NA
Trough level CsA, µg/L	178.3 (±45.9)	167.0 (±0.0)	NA
Daily dose FK, mg	5.8 (±3.6)	5.2 (±2.3)	0.50
Trough level FK, µg/L	8.0 (±2.5)	9.1 (±2.1)	0.11
Cytostatic regimen			
Patients on AZA/MMF, n (%)	22/2 (51.1/4.7)	20/4 (50.0/10.0)	0.38
Daily dose AZA, mg	50.0 (±28.9)	57.5 (±32.6)	0.43
Daily dose MMF, mg	1500.0 (±707.1)	1180.0 (±386.8)	0.49
Trough level MMF, mg/L	1.8 (±0.3)	2.6 (±0.9)	0.33
At 2 years			
Daily dose prednisolone, mg	4.1 (±0.5)	4.0 (±1.0)	0.62
CNI-regimen			
Patients on CSA/FK, n (%)	2/16 (4.7/37.2)	1/27 (2.5/67.5)	0.31
Daily dose CsA, mg	237.5 (±17.7)	225.0 (±0.0)	NA
Trough level CsA, µg/L	202.0 (±82.0)	182.0 (±)	NA
Daily dose FK, mg	5.8 (±3.8)	4.4 (±2.1)	0.12
Trough level FK, µg/L	8.9 (±2.0)	9.3 (±2.5)	0.54
Cytostatic regimen			
Patients on AZA/MMF, n (%)	13/2 (/)	17/2 (/)	0.80
Daily dose AZA, mg	56.7 (±32.5)	50.0 (±28.0)	0.55
Daily dose MMF, mg	2250.0 (±353.6)	610.0 (±155.6)	**0.027**
Trough level MMF, mg/L	1.9 (±0.7)	1.2 (±0.4)	0.29

Table S1 legend

Immunosupressive regimen during the study for the patients of the placebo-arm (n=43) and of the azithromycin-arm (n=40). Immunosuppressive regimen was assessed for each patient until study-discontinuation, reaching BOS or death within 2 years after LTx, or for the other patients until 2 years after LTx. Data are presented either as mean (±standard deviation) or as total value (percentage). Groups were compared using unpaired t-test or Chi-square test.

Abbreviations: rATG: rabbit anti-thymocyte globulin, CNI: Calcineurin inhibitor, CsA: cyclosporine A, FK: Tacrolimus (FK506), AZA**:** Azathioprine, MMF: mycophenolate mofetil, NA: not applicable.

Table S2: Spirometry and bronchoscopic procedures

	Placebo (n=43)	**Azithromycin** (n=40)	**p-value**
Spirometric procedures			
- Total, n	1059	1044	
- Mean per patient, n	24.6 (±7.6)	26.1 (±6.5)	p=0.29
Routine and clinically indicated bronchoscopic procedures			
- Total, n	268	256	
- Mean per patient, n	6.2 (±1.4)	6.4 (±1.6)	p=0.62
- Time from transplantation, days	205.4 (±100.8)	237.9 (±95.0)	p=0.14
- Bronchoalveolar return (mL/100mL)	41.2 (±8.0)	43.9 (±7.3)	p=0.13
Routine bronchoscopic procedures after study-inclusion			
- Total, n	199	198	
- Mean per patient, n	4.6 (±1.4)	4.9 (±1.5)	p=0.33
- Time from transplantation, days	226.8 (±104.2)	261.7 (±108.2)	p=0.15
- Bronchoalveolar return (mL/100mL)	41.8 (±8.5)	44.2 (±8.3)	p=0.21
Routine and clinically indicated transbronchial biopsies			
- Total, n	129	106	
- Mean per patient, n	3.0 (±1.0)	2.7 (±1.1)	p=0.14
- Time from transplantation, days	138.9 (±93.8)	112.0 (±92.1)	p=0.19
Routine transbronchial biopsies after study-inclusion			
- Total, n	75	69	
- Mean per patient, n	1.7 (±0.4)	1.7 (±0.5)	p=0.85
- Time from transplantation, days	57.4 (±20.0)	52.8 (±17.1)	p=0.27

Table S2 legend:

Spirometric and bronchoscopic procedures performed during the study for the patients of the placebo-arm (n=43) and of the azithromycin-arm (n=40). Spirometries and bronchoscopic procedures were assessed for each patient until study-discontinuation, reaching BOS or death within 2 years after LTx, or for the other patients until 2 years after LTx. Data are presented either as mean (±standard deviation) or as total value (percentage). Groups were compared using unpaired t-test.

Table S3: Secondary outcome parameters

	Placebo (n=43)	Azithromycin (n=40)	p-value
Acute rejection (grade A)			
- Cumulative score per patient	0.84 (±1.02)	0.87 (±0.82)	0.57
- Rate per patient per year	0.86 (±1.53)	0.78 (±1.17)	0.55
Grade A≥2 acute rejection			
- Cumulative score per patient	0.35 (±0.61)	0.47 (±0.72)	0.52
- Rate per patient per year	0.42 (±1.21)	0.43 (±0.98)	0.63
Lymphocytic bronchiolitis (grade B)			
- Cumulative score per patient	0.40 (±0.70)	0.20 (±0.52)	0.23
- Rate per patient per year	0.44 (±1.06)	0.16 (±0.49)	0.20
Grade B≥2 lymphocytic bronchiolitis			
- Cumulative score per patient	0.21 (±0.47)	0.07 (±0.35)	0.28
- Rate per patient per year	0.33 (±1.04)	0.08 (±0.44)	0.26
CMV pneumonitis.			
- Cumulative episodes per patient	0.26 (±0.58)	0.20 (±0.41)	0.99
- Rate per patient per year	0.41 (±1.18)	0.21 (±0.51)	0.99
Non-CMV pneumonitis			
- Cumulative episodes per patient	0.77 (±0.99)	0.73 (±1.11)	0.71
- Rate per patient per year	0.95 (±1.4)	0.73 (±1.42)	0.51
***P. aeruginosa* airway colonization**			
- Before the onset of BOS, n (%)	5 (11.6)	5 (12.5)	0.90
- At 2 years after transplantation, n (%)	14 (32.6)	12 (30.0)	0.80
Gastroesophageal reflux			0.74
- Present, n (%)	22 (51.2)	18 (45.0)	
- Absent, n (%)	18 (41.9)	20 (50.0)	
- Not assessed, n (%)	3 (6.8)	2 (5.0)	
- Time of assessment from transplantation, days	380.1 (±169.6)	342.8 (±172.1)	0.34

Table S3 legend

Secondary outcome parameters for the patients of the placebo-arm (n=43) and the azithromycin-arm (n=40). Acute rejection and lymphocytic bronchiolitis, CMV and non-CMV pneumonitis episodes were assessed for each patient until drop-out, reaching BOS or death within 2 years after LTx, or for the other patients until 2 years after LTx. Data are presented as mean (±standard deviation) or as total value (percentage). Groups were compared using unpaired t-test or Chi-square test.

Abbreviations: CMV: *cytomegalovirus*, A≥2: at least moderate acute rejection on histopathology, B≥2: at least moderate lymphocytic bronchiolitis on histopathology, *P. aeruginosa*: *Pseudomonas aeruginosa*.

Definitions: CMV-mismatch was defined as a CMV-positive donor and a CMV-negative recipient, CMV pneumonitis was defined either as increasing CMV PCR titers or biopsy-proven pulmonary CMV infection requiring anti-viral treatment. Non-CMV pneumonitis was defined as a bacterial or fungal pulmonary infection requiring in-hospital treatment with intravenous antibiotics or anti-fungal drugs. *P. aeruginosa* airway colonization was assessed by evaluating all respiratory specimens obtained by standardized cultured techniques as previously described (Vos *et al*. Eur Respir J 2008; 31(5):1037-45). Gastroesophageal reflux was assessed by standardized gastroscopy or pH-measurement during the first 2 years post-LTx.

Table S4: Open-label treatment

	Total group (n=83)	Placebo (n=43)	Azithromycin (n=40)	p-value
Patients entered in open-label azithromycin treatment, n (%)	23 (27.7)	18 (41.9)	5 (12.5)	
Time from transplantation to BOS, days	328.1 (±199.9)	344.1 (±197.0)	270.8 (±222.6)	0.48
BAL neutrophilia at BOS, %	33.8 (±32.4)	39.1 (±34.8)	18.2 (±18.1)	0.22
Change in FEV_1 after start of open-label treatment				0.65
- Response (improvement), n (% of open-label patients)	12 (52.2)	10 (55.6)	2 (40.0)	
- No response (stabilisation or deterioration), n (% of open-label patients)	10 (43.5)	7 (38.8)	3 (60.0)	
- Not assessable, n (%of all open-label patients)	1 (4.3)	1 (5.6)	0 (0.0)	
Responders vs. non-responders:				
Time from transplantation to BOS, days	235.5 (±151.2) vs. 446.2 (±205.7) *	251.7 (±154.9) vs. 488.1 (±185.4) *	154.5 (±140.7) vs. 348.3 (±258.2)	
FEV_1 at BOS				
- %pred	52.9 (±21.5) vs. 54.4 (±21.0)	54.7 (±25.1) vs. 53.0 (±21.8)	48.7 (±11.7) vs. 61.5 (±21.9)	
- L	1.6 (±0.8) vs. 1.6 (±0.8)	1.6 (±0.9) vs. 1.6 (±0.9)	1.5 (±0.6) vs. 1.5 (±0.7)	
BAL neutrophilia at BOS, %	53.3 (±33.4) vs. 12.5 (±12.8) **	57.7 (±32.2) vs. 11.3 (±14.1) **	23.1 (±30.4) vs. 14.9 (±12.2)	
Grade A rejection, rate per patient per year	2.0 (±2.5) vs. 1.2 (±1.2)	1.8 (±2.5) vs. 0.8 (±1.2)	3.5 (±2.9) vs. 1.9 (±0.9)	
Grade A≥2 rejection, rate per patient per year	1.3 (±2.5) 0.5 (±0.9)	1.0 (±2.3) vs. 0.3 (±0.9)	2.8 (±3.9) vs. 1.0 (±0.9)	
Grade B rejection, rate per patient per year	1.2 (±0.5) vs. 0.3 (±0.1)	1.2 (±1.9) vs. 0.2 (±0.4)	1.4 (±2.0) vs. 0.3 (±0.5)	
Grade B≥2 rejection, rate per patient per year	1.2 (±1.9) vs. 0.1 (±0.2)	1.2 (±1.9) vs. 0.1 (±0.2)	1.4 (±2.0) vs. 0.0 (±0.0)	
CMV infection, rate per patient per year	0.8 (±1.8) vs. 0.1 (±0.4)	1.0 (±1.9) vs. 0.2 (±0.4)	0.0 (±0.0) vs. 0.0 (±0.0)	
Non-CMV infection, rate per patient per year	1.9 (±2.0) vs.1.3 (±1.6)	2.2 (±2.0) vs. 0.8 (±1.5)	0.0 (±0.0) vs. 2.3 (±2.5)	
***P. aeruginosa* colonization, n**	4/12 vs. 4/10	3/10 vs. 1/7	1/2 vs. 3/3	
Gastroesophageal reflux present, n	5/12 vs. 5/10	4/10 vs. 3/7	1/2 vs. 2/3	
New FEV_1 deterioration due to BOS after initial response in FEV_1, n	3/12	2/10	1/2	0.29
Mortality (responders vs. non-responders), n	2/12 vs. 5/10	2/10 vs. 3/7	0/2 vs. 2/3	

Table S4 Legend

Evaluation according to change in FEV_1 after 3 to 6 months of open-label treatment with azithromycin for BOS for all patients (n=83), the patients of the placebo-arm (n=43) and the azithromycin-arm (n=40). Responders had an improvement in FEV_1 of 10% or more and non-responders of less than 10% compared to start of azithromycin. Change in FEV_1 over time is also represented in supplementary Figure S1. Data are presented as mean (±standard deviation) or as total value (percentage). Groups were compared using unpaired t-test or Chi square-square test, * $p<0.05$, ** $p<0.01$ for responders compared to non-responders.

VI Supplementary Figures

Figure S1

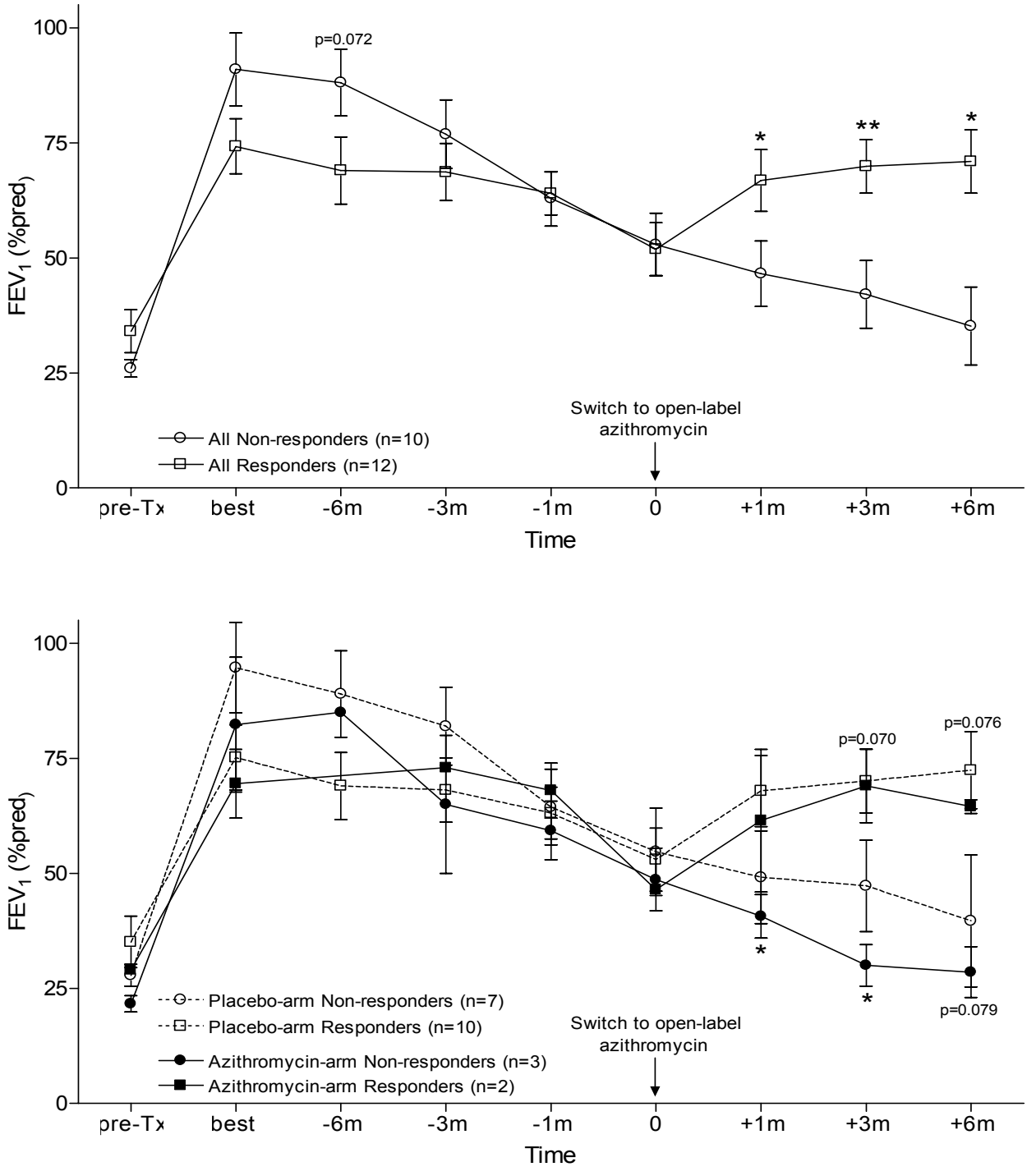

Figure S1 Legend

Evaluation according to change in FEV_1 after 3 to 6 months of open-label treatment with azithromycin for BOS for all patients (n=83), the patients of the placebo-arm (n=43) and the azithromycin-arm (n=40). Responders (n=12) were defined as having an improvement in FEV_1 of 10% or more and non-responders (n=10) of less than 10% compared to start of azithromycin. In all responders FEV_1 improved to BOS stage 0 after 3 to 6 months of open-label treatment. Dots or squares represent means and error bars SEM. Reponders an non-responders were compared using unpaired t-test, * $p<0.05$, ** $p<0.01$