ONLINE SUPPLEMENTARY DATA

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Transplant monitoring

After discharge, LTx recipients received routine follow-up at fixed time points: twice a week during the first 2-4 weeks after discharge, then once weekly until 12 weeks after LTx, every 4 weeks until 6 months after LTx, every 6-8 weeks until 12 months after LTx, and thereafter life-long at intervals of 3-4 months. In addition, patients performed home spirometry and were instructed to come to the outpatient clinic in case of fever or >10% FEV_1 decline. During each patient contact, complete history and physical examination was performed as well as blood, urine, sputum and pharyngeal swab cultures, spirometry and chest radiography. In addition, chest CT and bronchoscopic evaluation with broncho-alveolar lavage (BAL), transbronchial biopsies (TBB) and/or endobronchial biopsies were performed at discharge and 3, 6, 12, 18 and 24 months after LTx, and whenever clinically indicated. When a FEV_1 decline of ≥ 20% was noticed, chest CT and bronchoscopy with BAL and TBB were performed to exclude acute causes for pulmonary function decline.

Therapeutic management

Following induction therapy with anti-thymocyte globulin (rATG) (3 mg/kg/d for 3 days), patients received conventional triple-drug immunosuppressive maintenance therapy consisting of methylprednisolone, a cytostatic agent (azathioprine or mycophenolate mofetil) and a calcineurin inhibitor (cyclosporine A or tacrolimus). Drug choice was made according to the discretion of the treating clinician, dose adjustments were made based on renal function and immunosuppressive trough levels. Acute rejection (grade A2 or higher) was treated by high dose corticosteroids during 3 days, tapered to oral maintenance dose over the next 2 to 3 weeks. Grade A1 acute rejection was treated by augmenting oral steroids, similarly followed by tapering. Isolated grade B rejection was treated with azithromycin (250 mg/day, trice weekly) and corticosteroids in case of ≥B2R similar to the protocol of acute rejection.

In suspected CLAD, immunosuppressive treatment was optimized if possible and azithromycin (250 mg/day, trice weekly) was initiated. In established, progressive CLAD, treatment with montelukast (MLK) 10 mg/day was started. In case of subsequent CLAD progression (i.e. further decline in FEV_1 after ≥ 3-6 months of MLK), rescue-treatment with pulsed steroids, rATG, TLI, pirfenidone, antibody-directed therapy (pulsed methylprednisolone, followed by plasmapheresis, intravenous immunoglobulins (IVIG) and rituximab since 2013), or retransplantation was performed in selected cases, based on the treating physician's discretion. Extracorporeal photopheresis (ECP) is not commonly available in our center for CLAD.

In addition, all LTx recipients were routinely treated with a low dose proton pomp inhibitor. If reflux was diagnosed after LTx by either pH impedance measurement or gastroscopy, low dose proton pump inhibitor was switched to high dose proton pump inhibitor. None of the included patients underwent fundoplication surgery after LTx.

After LTx, conventional infectious prophylaxis for cytomegalovirus, Aspergillus spp., and Pneumocystis spp was started. CMV-related disease or pneumonitis was treated with intravenous ganciclovir (5 mg/kg twice daily for at least two weeks or lower based on eGFR); Aspergillus infection was treated with voriconazole (4 mg per kg bid IV). Antibiotic treatment for bacterial infection after LTx was guided using bacteriologic cultures.

Supplementary tables

Table S1. Number of samples in successfully and unsuccessfully PA eradicated patients

	Successful eradication	**Unsuccessful eradication**	**p-value**
Respiratory samples per patient, n	8 (5-12)	7 (4-11)	0.45
PA pos respiratory samples, n	2 (1-3)	4 (2-6)	**0.0005**
PA neg respiratory samples, n	6 (3-10)	3 (1-7)	**0.04**
Sputum samples per patient, n	3 (1-7)	3 (2-5)	0.96
PA pos sputum samples, n	1 (0-2)	2 (0-4)	**0.03**
PA neg sputum samples, n	2 (0-6)	1 (0-3)	0.30
BAL samples per patient, n	5 (2-6)	3 (1-5)	0.96
PA pos BAL samples, n	1 (0-2)	1 (0-2)	0.18
PA neg BAL samples, n	4 (1-5)	0 (1-4)	**0.02**

Table S1. Number of positive and negative respiratory (sputum and BAL), sputum and BAL samples in successfully and unsuccessfully *PA* eradicated patients.

Table S2. Eradication regimen

	Successful eradication	**Unsuccessful eradication**	**p-value**
Patients, n (%)	76 (80%)	19 (20%)	
Eradication Treatment, n (%)	53	13	**0.02**
IV antibiotics	31 (58%)	13 (100%)	
IV and PO antibiotics	7 (13%)	0 (0%)	
PO antibiotics	15 (28%)	0 (0%)	
No eradication treatment	23	6	
IV antibiotics, n (%)			
Ceftazidime	8 (21%)	4 (31%)	0.48
Colistin	6 (16%)	5 (38%)	0.09
Meropenem	18 (47%)	9 (69%)	0.17
Piperacillin/tazobactam	19 (50%)	3 (23%)	0.09
Tobramycin	16 (42%)	4 (31%)	0.47
Combination treatment	25 (66%)	10 (77%)	0.46
Days of IV antibiotics, days	14 (10-17)	14 (10-21)	0.90
PO antibiotics, n (%)			
Levofloxacin	12 (82%)	0 (0%)	NA
Ciprofloxacin	8 (36%)	0 (0%)	NA
Moxifloxacin	2 (9%)	0 (0%)	NA
Days of PO antibiotics, days	14 (9-14)	NA	NA

Table S2. Eradication treatment in successfully versus unsuccessfully *PA* eradicated patients. Inhaled antibiotics are not routinely used because they are not reimbursed after LTx in Belgium.

Supplementary legend to figure 4

At 01/01/2013, 11 of the included LTx patients were successfully *PA* eradicated (of which 1 was already diagnosed with CLAD), 4 were unsuccessfully *PA* eradicated (of which none were diagnosed with CLAD) and 80 were not transplanted, had no positive *PA* sample yet or already died. Successfully *PA* eradicated patients had a significantly better CLAD-free survival (p=0.017) and tended to have a better graft survival (p=0.062) compared to unsuccessfully *PA* eradicated patients (figure 4A and 4E).

At 01/01/2014, 23 of the included LTx patients were successfully *PA* eradicated (of which 2 were diagnosed with CLAD), 6 were unsuccessfully *PA* eradicated (of which 2 were diagnosed with CLAD) and 66 were not transplanted, had no positive *PA* sample yet or already died. Successfully *PA* eradicated patients tended to have a better CLAD-free survival (p=0.17, figure 4B) and had a better graft survival (p=0.004, figure 4F) compared to unsuccessfully *PA* eradicated patients.

At 01/01/2015, 32 of the included LTx patients were successfully *PA* eradicated (of which 6 were diagnosed with CLAD), 8 were unsuccessfully *PA* eradicated (of which 4 were diagnosed with CLAD) and 55 were not transplanted, had no positive *PA* sample yet or already died. Successfully *PA* eradicated patients had a significantly better graft survival compared to unsuccessfully *PA* eradicated patients (p<0.0001, figure 4G). There was no significant difference in CLAD-free survival between both groups (p=0.37, figure 4C).

At 01/01/2016, 45 of the included LTx patients were successfully *PA* eradicated (of which 10 were diagnosed with CLAD), 9 were unsuccessfully *PA* eradicated (of which 2 were diagnosed with CLAD) and 41 were not transplanted, had no positive *PA* sample yet or already died. Successfully *PA* eradicated patients had a significantly better CLAD-free (p=0.01, figure 4D) and graft survival (p<0.0001, figure 4H) compared to unsuccessfully *PA* eradicated patients (p<0.0001).