Five-year outcome of an early everolimus-based quadruple immunosuppression in lung transplant recipients: follow-up of the 4EVERLUNG study

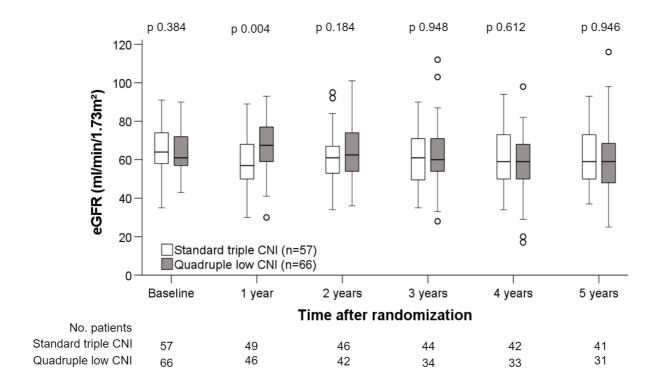
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Supplementary Table 1. Characteristics of patients in whom the assigned regimen was switched compared to the per protocol population.

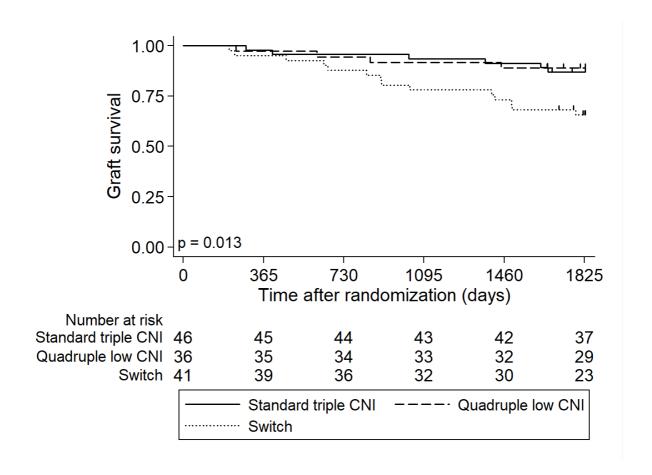
Characteristics	Triple n=46 (37)	Quadruple n=36 (29)	Switch n=41 (33)	P
Gender (female), n (%)	17 (37)	15 (42)	13 (32)	0.662
Age (y), median (25th, 75th percentile)	56 (50, 61)	59 (49, 61)	58 (53, 60)	0.910
Primary diagnosis, n (%)				0.749
Obstructive	20 (43)	15 (42)	19 (46)	
Restrictive	22 (48)	16 (44)	20 (49)	
Cystic fibrosis	4 (9)	5 (14)	2 (5)	
Thromboembolism pre randomization, n (%)	2 (5)	2 (6)	3 (8)	0.839
CMV risk status pre randomization, n (%)				0.117
Low risk, D-R-	8 (17)	7 (20)	12 (29)	
Intermediate risk, R+	30 (65)	20 (56)	17 (42)	
High risk, D+R-	8 (17)	8 (23)	12 (29)	
Donor-specific antibodies post randomization, n (%)	5 (11)	1 (3)	9 (22)	0.035
No. of acute rejections (≥A1) post randomization, n (%)	2 (4)	2 (6)	14 (34)	< 0.001
Dialysis, n (%)	-	-	3 (7)	0.050
D 1, (0/)				
Renal transplant, n (%)	-	-	-	
Malignancy, n (%)	- 7 (15)	- 8 (22)	- 7 (17)	0.704
• • •	7 (15) 5 (11)	8 (22) 8 (22)	- 7 (17) 9 (22)	0.704 0.292
Malignancy, n (%)				
Malignancy, n (%) Thrombotic events post randomization, n (%)	5 (11)	8 (22)	9 (22)	0.292
Malignancy, n (%) Thrombotic events post randomization, n (%) CMV infection, n (%)	5 (11) 19 (41)	8 (22) 9 (25)	9 (22) 19 (46)	0.292 0.136
Malignancy, n (%) Thrombotic events post randomization, n (%) CMV infection, n (%) CMV hospitalizations, n (%)	5 (11) 19 (41) 3 (7)	8 (22) 9 (25) 1 (3)	9 (22) 19 (46) 6 (15)	0.292 0.136 0.145
Malignancy, n (%) Thrombotic events post randomization, n (%) CMV infection, n (%) CMV hospitalizations, n (%) Community-acquired respiratory viral infections, n (%)	5 (11) 19 (41) 3 (7) 16 (35)	8 (22) 9 (25) 1 (3) 12 (33)	9 (22) 19 (46) 6 (15) 21 (51)	0.292 0.136 0.145 0.188
Malignancy, n (%) Thrombotic events post randomization, n (%) CMV infection, n (%) CMV hospitalizations, n (%) Community-acquired respiratory viral infections, n (%) No. of hospitalizations, median (25th, 75th percentile)	5 (11) 19 (41) 3 (7) 16 (35) 1 (0, 2)	8 (22) 9 (25) 1 (3) 12 (33) 1 (0,3)	9 (22) 19 (46) 6 (15) 21 (51) 2 (1, 5)	0.292 0.136 0.145 0.188 0.005
Malignancy, n (%) Thrombotic events post randomization, n (%) CMV infection, n (%) CMV hospitalizations, n (%) Community-acquired respiratory viral infections, n (%) No. of hospitalizations, median (25th, 75th percentile) Hospitalization days, median (25th, 75th percentile)	5 (11) 19 (41) 3 (7) 16 (35) 1 (0, 2) 9 (0, 22)	8 (22) 9 (25) 1 (3) 12 (33) 1 (0,3) 6 (0,28)	9 (22) 19 (46) 6 (15) 21 (51) 2 (1, 5) 21 (5, 49)	0.292 0.136 0.145 0.188 0.005 0.009
Malignancy, n (%) Thrombotic events post randomization, n (%) CMV infection, n (%) CMV hospitalizations, n (%) Community-acquired respiratory viral infections, n (%) No. of hospitalizations, median (25th, 75th percentile) Hospitalization days, median (25th, 75th percentile) Hospitalization for bacterial /fungal infections, n (%)	5 (11) 19 (41) 3 (7) 16 (35) 1 (0, 2) 9 (0, 22) 14 (30)	8 (22) 9 (25) 1 (3) 12 (33) 1 (0, 3) 6 (0, 28) 9 (25)	9 (22) 19 (46) 6 (15) 21 (51) 2 (1, 5) 21 (5, 49) 16 (39)	0.292 0.136 0.145 0.188 0.005 0.009

Bronchiolitis obliterans syndrome	8 (17)	4 (11)	4 (10)	0.365
Restrictive allograft syndrome	2 (4)	-	4 (10)	
Mixed	2 (4)	1 (3)	5 (12)	
Undefined / unclassified	2 (4)	-	1 (2)	
Re-do lung transplant, n (%)	2 (4)	-	-	0.182
Deceased, n (%)	5 (11)	4 (11)	14 (34)	0.008
Cause of death, n (%)				0.118
Unknown	1 (2)	-	-	
CLAD	3 (7)	1 (3)	8 (20)	
Infection	-	-	3 (7)	
Malignancy	-	1 (3)	1 (2)	
Cardiovascular	1 (2)	2 (6)	-	
Other	-	-	2 (5)	

Data are presented as median (25^{th} , 75^{th} percentile) and number and percentage, respectively. List of abbreviations: CMV, Cytomegalovirus; CLAD, chronic lung allograft dysfunction.



Supplementary Figure 1. Estimated glomerular filtration rate over the observation period according the actual regimen. Patients are represented in the respective group until the actual switch. Abbreviation of definitions: CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate formula; ITT, intention to treat; PP, per protocol.



Supplementary Figure 2. Graft-survival by Kaplan Meier analysis in patients switched to an alternative regimen compared to the PP population. Abbreviation of definitions: CNI, calcineurin inhibitor; PP, per protocol.