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### Conversion from calcineurin inhibitor- to belatacept-based maintenance immunosuppression in renal transplant recipients: a randomized phase 3b trial

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**IM103-116 investigators and recruitment numbers.**

Country	Investigator	Affiliation	Patients enrolled, n
United States	Rohini Prashar	Henry Ford's Transplant Institute	53
Germany	Hermann Haller	MHH—Medizinische Hochschule Hannover; Klinik fuer Nieren und Hochdruckerkrankungen	49
Germany	Klemens Budde	Charité—Universitaetsmedizin Berlin—Campus Charité Mitte (CCM)	35
Argentina	Maria C. Vazquez	Sanatorio Parque Rosario	27
France	Nassim Kamar	CHU Rangueil	18
United States	Arjang Djamali	University of Wisconsin School of Medicine and Public Health	18
United States	Avinash Agarwal	University of Virginia Health System	17
Netherlands	Johan W. de Fijter	Leids Universitair Medisch Centrum (LUMC)	16
Argentina	Maria C. Rial	Instituto de Nefrologia, Nephrology S.A.	15
France	Lionel Rostaing	Centre Hospitalier Universitaire de Grenoble-Hôpital Albert Michallon	15
United States	Nicolae Leca	University of Washington Medical Center	15
Argentina	Luis Gaité	Clínica de Nefrología, Urología y Enfermedades Cardiovasculares	14
Netherlands	Stefan P. Berger	University Medical Center Groningen	14
United States	Debra L. Sudan	Duke University Medical Center	13
Colombia	Camilo Montero	Clínica Colsanitas S.A. Sede Clínica Universitaria Colombia	12
United States	Richard Knight	The Methodist Hospital	12
United States	Stephen Jensik	RUSH University Transplant Program	12
United States	Thomas McCune	Sentara Norfolk General Hospital	11
United States	Sanjay Kulkarni	Yale Medical Group	11
Austria	Bruno Watschinger	Medizinische Universität Wien AKH - Allgemeines Krankenhaus Wien	10
United States	Flavio Vincenti	UCSF Medical Center	10
Austria	Karl Lhotta	Academic Teaching Hospital Feldkirch	9
Germany	Oliver Witzke	Universitaetsklinikum Essen, Klinik fuer Nephrologie, Medizinisches Forschungszentrum	9
Germany	Bernhard Banas	University Hospital Regensburg	8
Germany	Michael Wiesener	Klinikum Erlangen der Friedrich-Alexander-Universitaet Erlangen-Nuernberg	8
United States	Stephan Pastan	Emory University	8
United States	John Vella	Maine Transplant Program	8
United States	Samer H. Bani Hani	Providence Sacred Heart Medical Center and Children's Hospital	8
United States	Shirley Shwu-Shiow Chang	University of Buffalo	8
Argentina	Rafael Maldonado	Clínica Privada Vélez Sarsfield	7
Argentina	Ruben Schiavelli	Hospital General de Agudos Dr. Cosme Argerich	7
Argentina	Gervasio Soler Pujol	CEMIC Las Heras Hospital	7
United States	Arman Faravardeh	California Institute of Renal Research	7

Country	Investigator	Affiliation	Patients enrolled, n
Argentina	Jorge De La Fuente	Hospital Privado Centro Médico de Cordoba S.A.	6
Argentina	Pablo Raffaele	Fundación Favalaro, Hospital Universitario Fundación Favalaro	6
France	Pierre Merville	Hôpital Pellegrin-Tripode Département Néphrologie	6
Germany	Thorsten Feldkamp	Universitaetsklinikum Schleswig-Holstein Campus Kiel	6
Netherlands	S.A. Nurmohamed	VU University Medical Center	6
United States	Paul Bolin	East Carolina University Nephrology Clin Research Lab	6
United States	Mohamed Ahmed El-Ghoroury	St. Clair Nephrology Research, St. John Medical Center— Renaissance Renal Research Institute	6
United States	Tariq Shah	Transplant Research Institute	6
United States	Bernard Fischbach	Baylor All Saints Medical Center at Ft. Worth	6
Austria	Gert Mayer	Universitätsklinik Innsbruck	5
France	Antoine Durrbach	APHP Bicêtre Hospital, Nephrology Department	5
France	Dominique Bertrand	Hospital Center University Rouen	5
Switzerland	Uyen Huynh-Do	INSELSPITAL Bern, Universitaetsspital Bern Departement DURN Klinik fuer Nephrologie, Hypertonie und Klinische Pharmakologie	5
United States	Bradley Marder	Denver Nephrologists, PC	5
United States	Harold Helderman	Vanderbilt University Medical Center, GI Research Office	5
Argentina	Federico Cicora	Hospital Aleman	4
France	Yannick Le Meur	CHU de Brest, Centre d'investigation clinique, Hôpital De La Cavale Blanche	4
Germany	Bernd Krueger	University Hospital Mannheim	4
Germany	Barbara Suwelack	University Hospital of Muenster, UKM Med D TX Nephrology	4
Germany	Lutz Renders	Klinikum Rechts der Isar der Technischen Universitaet Muenchen	4
United States	Ram Peddi	California Pacific Medical Center, Department of Transplantation	4
United States	Kim M. Rice	Baylor University Medical Center	4
France	Emmanuel Morelon	Hôpital Edouard Herriot	3
Germany	Ingeborg A. Hauser	Universitaetsklinik der Johann Wolfgang Goethe- Universitaet	3
United States	Ehab Saad	Medical College of WI Froedtert Hospital	3
United States	Maria Aurora Posadas Salas	Medical University of South Carolina, SCTR Research Nexus	3
United States	Yasir Qazi	Keck Medical Center of USC	3
United States	Karthik Ranganna	Drexel University College of Medicine	3
United States	Brian Gallay	UC Davis Heart Center, University California-Davis Medical Center, University of California, San Francisco (UCSF)- Kidney Transplant Service	3
United States	Harold Yang	Central PA Transplant Foundation	3

Country	Investigator	Affiliation	Patients enrolled, n
United States	Stanley Jordan	Cedars-Sinai Medical Center	3
United States	Gaurav Gupta	Virginia Commonwealth University, Virginia Commonwealth University Medical Center	3
Austria	Alexander Rosenkranz	Universitätsklinikum Graz	2
Germany	Kai Lopau	University of Wuerzburg	2
Netherlands	Luuk B. Hilbrands	Radboud University Nijmegen Medical Centre	2
United States	Winfred W. Williams	Massachusetts General Hospital	2
United States	Rafael Villicana	Loma Linda University Medical Center (LLUMC), Children's Hospital, Transplantation Institute	2
United States	Fuad Shihab	University of Utah, Department of Nephrology	2
United States	Nelson B. Goes	Swedish Medical Center, Swedish Organ Transplant and Liver Center	2
United States	Alexander Wiseman	University of Colorado Denver	2
United States	Suphamai Bunnapradist	UCLA Kidney Transplant Research Office	2
United States	Clifford Miles	University of Nebraska Medical Center	2
France	Bruno Moulin	NOUVEL HÔPITAL CIVIL Service Néphrologie et Hémodialyse	1
France	Philippe Grimbert	Centre Hospitalier Universitaire (CHU)—Hôpital Henri Mondor	1
France	Denis Glotz	Hôpital Saint Louis	1
Germany	Claudia Sommerer	Nierenzentrum Heidelberg	1
Norway	Sadollah Abedini	Vestfold Hospital Trust	1
Sweden	Lars Mjornstedt	Sahlgrenska University Hospital	1
United States	Reginald Y. Gohh	Rhode Island Hospital	1
United States	Daniel Katz	University of Iowa Health Care	1
United States	Hasan Ahmad Khamash	Mayo Clinic Hospital	1
United States	Anil S. Paramesh	Tulane University Health Sciences Center	1
Argentina	Carlos Antonio Balaguer	Hospital Español De Mendoza	0
Argentina	Hugo S. Petrone	Crai Sur	0
Austria	Peter Neudorfer	Krankenhaus der Elisabethinen Linz GmbH	0
Colombia	Liliana Mesa	Valle del Lili	0
Colombia	Carlos Benavides	Fundación Cardioinfantil	0
Colombia	Paola Garcia	Hospital Universitario San Ignacio	0
France	Christophe Legendre	Hôpital Necker et Université Descartes	0
Germany	Christian Hugo	Universitätsklinikum Carl Gustav Carus	0
Germany	Martin Nitschke	Universitätsklinikum Schleswig-Holstein, Campus Luebeck	0
Germany	Bjoern Nashan	Universitätsklinikum Hamburg-Eppendorf Klinik für Hepatobiliäre Chirurgie und Transplantationschirurgie	0
Germany	Markus van der Giet	Charité Mitte, Transplantationszentrum Benjamin Franklin	0
Germany	Bernd Schroppel	Universitätsklinikum Ulm	0

Country	Investigator	Affiliation	Patients enrolled, n
Netherlands	Frederike J. Bemelman	Academic Medical Center	0
Netherlands	Arjan D. Van Zuilen	UMC Utrecht	0
Norway	Hallvard Holdaas	OUS	0
Sweden	Lars Backman	Uppsala University Hospital	0
Sweden	Jonas Wadstrom	Karolinska University Hospital	0
Switzerland	Rudolf Wuethrich	UniversitaetsSpital Zuerich (University Hospital Zurich)	0
Switzerland	Karine Hadaya	Geneva University Hospital, Department of Nephrology and Transplantation	0
Switzerland	Dela Golshayan	CHUV	0
United States	Sander Florman	Recanati/Miller Transplantation Institute	0
United States	Roy Bloom	Penn Medicine, University of PA Health System	0
United States	Viktor Bowers	Tampa General Medicine Group	0
United States	Donald E. Hricik	University Hospitals Cleveland Medical Center	0
United States	Richard Fatica	Cleveland Clinic	0
United States	Paul F. Gores	Carolinas Medical Center	0
United States	Anil Chandraker	Brigham and Women's Hospital	0
United States	Sundaram Hariharan	University of Pittsburgh Medical Center	0
United States	Bobby Nibhanupudy	Florida Hospital Transplant Institute	0
United States	Roslyn B. Mannon	UAB Division of Nephrology	0
United States	Luis Campos	Methodist University Hospital Transplant Institute	0
United States	Daniel Brennan	Washington University School of Medicine	0
United States	Anup Patel	Saint Barnabas Medical Center	0
United States	Ronald Cotton	Baylor College of Medicine, St Luke's Health System, Kidney Transplant Clinic	0
United States	Anne Kruk	Central Pharmacy	0
United States	John (Steve) Bynon	Memorial Hermann—Texas Medical Center (TMC), The University of Texas Medical School at Houston	0
United States	Mark Stegall	Mayo Clinic	0
United States	Neema Stephens	University Transplant Center University of Texas—San Antonio	0
United States	Carlos F. Zayas-Montalvo	Medical College of Georgia at Augusta University	0
United States	Malcolm MacConmara	UT Southwestern Medical Center	0
United States	Martin Mai	Mayo Clinic	0

**Supplemental Table S1.** Baseline serum creatinine concentrations (mg/dL) by baseline eGFR and race.

Group	Race	Baseline eGFR stratified groups (mL/min/1.73 m <sup>2</sup> )					
		<45		45 to <60		≥60	
		n	Mean serum creatinine (mg/dL)	n	Mean serum creatinine (mg/dL)	n	Mean serum creatinine (mg/dL)
All patients	Black	17	2.11 (0.21)	20	1.62 (0.23)	11	1.31 (0.15)
	Non-Black	141	1.72 (0.27) <sup>a</sup>	163	1.35 (0.19)	94	1.10 (0.14)
Belatacept	Black	12	2.06 (0.22)	8	1.58 (0.24)	4	1.34 (0.12)
	Non-Black	75	1.72 (0.28)	78	1.34 (0.18)	46	1.11 (0.14)
CNI	Black	5	2.22 (0.15)	12	1.64 (0.23)	7	1.30 (0.17)
	Non-Black	66	1.71 (0.27) <sup>a</sup>	85	1.37 (0.20)	48	1.10 (0.14)

Data are mean (SD) unless otherwise stated. CNI, calcineurin inhibitor; SD, standard deviation.

<sup>a</sup>For 1 patient, the observed values were recorded as SI units (umol/L) and were converted into US units (mg/dL)

**Supplemental Table S2.** Serum trough concentrations of tacrolimus and cyclosporine at study entry (all patients) and during the trial period (CNI continuation arm only).

	n	Tacrolimus <sup>a</sup> (ng/mL)	n	Cyclosporine (ng/mL)
<b>Baseline concentrations at study entry</b>				
All patients	397	6.27 (2.31)	48	104.89 (87.98)
Belatacept conversion	199	6.35 (2.54)	23	127.91 (109.73)
CNI continuation	198	6.18 (2.05)	25	83.71 (56.09)
<b>Concentrations during the trial period (CNI continuation arm only)<sup>b</sup></b>				
Week 4	123	5.80 (1.73)	22	93.31 (89.86)
Week 12	129	5.88 (2.00)	20	99.34 (82.74)
Week 24	139	6.05 (3.49)	17	107.18 (100.31)
Week 36	134	5.82 (2.18)	17	105.47 (79.16)
Week 52	138	5.82 (2.50)	19	106.62 (80.92)
Week 76	111	5.96 (2.76)	14	87.84 (16.62)
Week 104	136	5.91 (3.06)	15	80.89 (19.18)

Data are mean (SD). CNI, calcineurin inhibitor; SD, standard deviation.

<sup>a</sup>Pre-randomization baseline data were unavailable for one patient.

<sup>b</sup>Concentrations provided are for patients who received at least one study drug dose and had at least one pharmacokinetic sample post-baseline.

**Supplemental Table S3.** Patient and graft survival at 24 months in patient subgroups.

	<b>Belatacept Conversion</b>	<b>CNI Continuation</b>
All patients	219/223 (98%)	217/223 (97%)
Recipient sex		
Male	147/150 (98%)	147/151 (97%)
Female	72/73 (99%)	70/72 (97%)
Recipient race		
White	187/191 (98%)	182/187 (97%)
Black	24/24 (100%)	24/24 (100%)
Geographic region		
North America	89/91 (98%)	94/94 (100%)
South America	35/35 (100%)	33/37 (89%)
Europe	95/97 (98%)	90/92 (98%)
Recipient age, yr		
<50	79/80 (99%)	79/83 (95%)
≥50	140/143 (98%)	138/140 (99%)
Donor age, yr		
<50	108/110 (98%)	109/111 (98%)
≥50	111/113 (98%)	108/112 (96%)
End stage renal disease (diabetes)		
Yes	36/38 (95%)	29/30 (97%)
No	183/185 (99%)	188/193 (97%)
Initial CNI treatment		
Cyclosporine	22/23 (96%)	23/25 (92%)
Tacrolimus	197/200 (98%)	194/198 (98%)
Baseline eGFR (mL/min/1.73 m <sup>2</sup> )		
<45	87/87 (100%)	68/71 (96%)
45–<60	84/86 (98%)	94/97 (97%)
≥60	48/50 (96%)	55/55 (100%)
Time from transplantation to randomization, mo		
6–12	69/70 (99%)	67/70 (96%)
>12	150/153 (98%)	150/153 (98%)

Data are n/N (%), where n refers to the number of events (patients surviving with functional grafts) and N refers to the number of patients within the subgroup.

CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate.



**Supplemental Table S4.** BPAR at 24 months in patient subgroups.

	<b>Belatacept Conversion</b>	<b>CNI Continuation</b>
All patients	18/223 (8%)	9/223 (4%)
Recipient sex		
Male	11/150 (7%)	5/151 (3%)
Female	7/73 (10%)	4/72 (6%)
Recipient race		
White	14/191 (7%)	7/187 (4%)
Black	3/24 (12%)	2/24 (8%)
Geographic region		
North America	7/91 (8%)	2/94 (2%)
South America	1/35 (3%)	3/37 (8%)
Europe	10/97 (10%)	4/92 (4%)
Recipient age, yr		
<50	5/80 (6%)	6/83 (7%)
≥50	13/143 (9%)	3/140 (2%)
Donor age, yr		
<50	4/110 (4%)	4/111 (4%)
≥50	14/113 (12%)	5/112 (4%)
End stage renal disease (diabetes)		
Yes	3/38 (8%)	1/30 (3%)
No	15/185 (8%)	8/193 (4%)
Initial CNI treatment		
Cyclosporine	0/23 (0)	1/25 (4%)
Tacrolimus	18/200 (9%)	8/198 (4%)
Baseline eGFR (mL/min/1.73 m <sup>2</sup> )		
<45	8/87 (9%)	3/71 (4%)
45–<60	6/86 (7%)	4/97 (4%)
≥60	4/50 (8%)	2/55 (4%)
Time from transplantation to randomization, mo		
6–12	6/70 (9%)	3/70 (4%)
>12	12/153 (8%)	6/153 (4%)

Data are n/N (%), where n refers to the number of events (BPAR) and N refers to the number of patients within the subgroup.

BPAR, biopsy-proven acute rejection; CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate.

**Supplemental Table S5.** Improvement from baseline in eGFR.<sup>a</sup>

	<b>Belatacept Conversion (n=223)</b>	<b>CNI Continuation (n=223)</b>
12 months		
5% improvement	119 (53)	64 (29)
10% improvement	98 (44)	48 (22)
24 months		
5% improvement	121 (54)	66 (30)
10% improvement	108 (48)	49 (22)

Data are n (%).

CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate.

<sup>a</sup>Values with imputation were identical to those without imputation.

**Supplemental Table S6.** Urine protein-to-creatinine ratio at baseline and at month 24.

Urine protein (mg)/ creatinine (mg)	Belatacept Conversion (n=223)		CNI Continuation (n=223)	
	Baseline	Month 24	Baseline	Month 24
<0.5	218/222 (98%)	166/188 (88%)	215/221 (97%)	157/169 (93%)
0.5–1.0	4/222 (2%)	17/188 (9%)	4/221 (2%)	8/169 (5%)
>1.0	0	5/188 (3%)	2/221 (1%)	4/169 (2%)
Missing	1/223 (<1%)	35/223 (16%)	2/223 (1%)	54/223 (24%)

Data are n/N (%), where N refers to the denominator used to calculate the percentages.

CNI, calcineurin inhibitor.

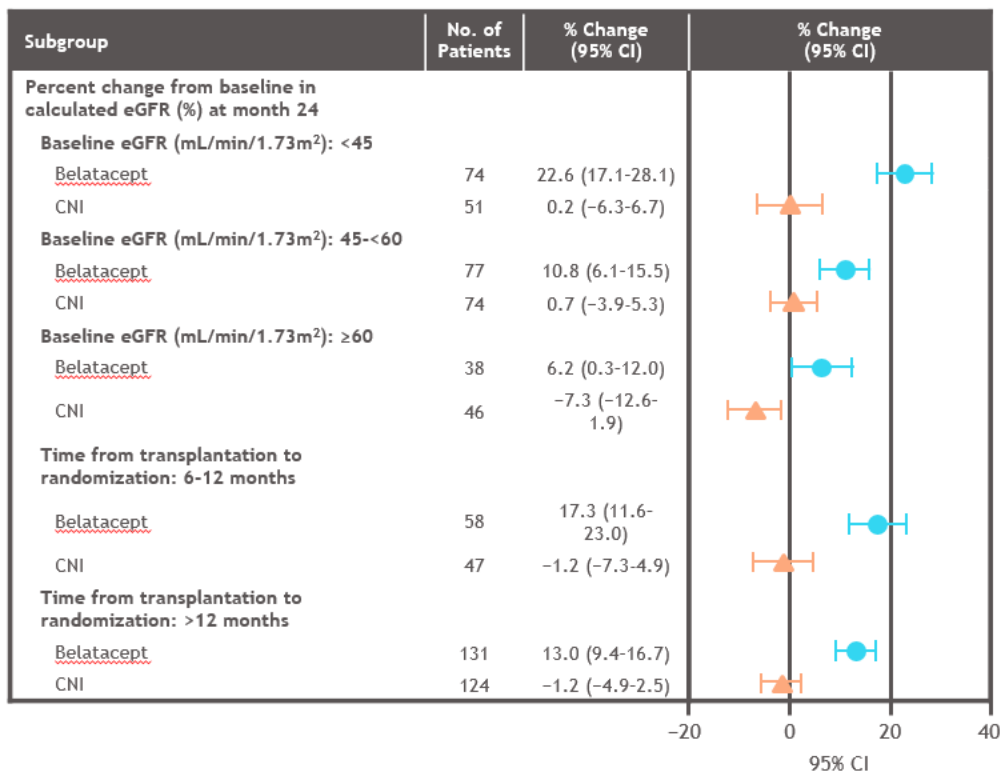
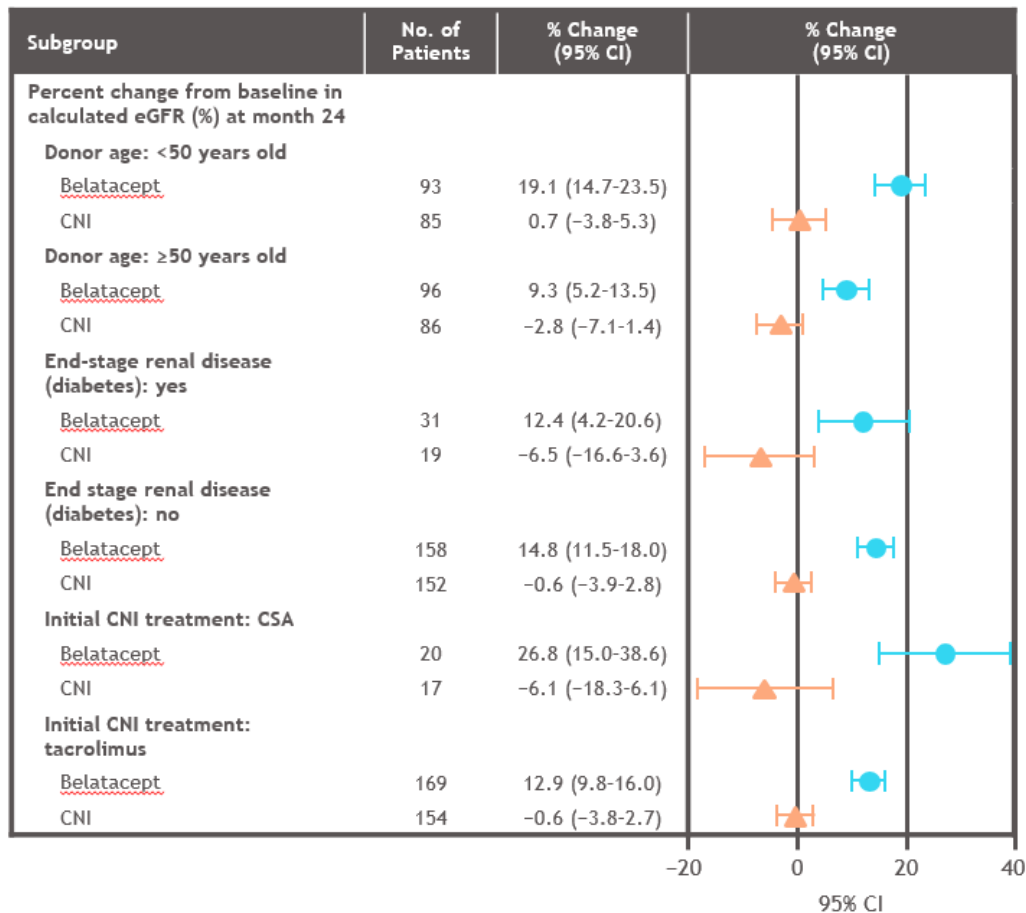
**Supplemental Table S7.** Impact on donor-specific antibodies.

	Belatacept Conversion (n=207)				CNI Continuation (n=199)			
	Class I	Class II	Class I and II	Total	Class I	Class II	Class I and II	Total
Pre-existing DSAs at baseline	3 (1%)	10 (5%)	3 (1%)	10 (5%)	15 (8%)	13 (7%)	2 (1%)	26 (13%)
<i>De novo</i> DSAs								
Month 12	2 (1%)	0	0	2 (1%)	4 (2%)	8 (4%)	3 (2%)	9 (5%)
Month 24	2 (1%)	0	0	2 (1%)	6 (3%)	12 (6%)	4 (2%)	14 (7%)

Data are n (%).

CNI, calcineurin inhibitor; DSA, donor-specific antibody.





**Supplemental Figure S2.** Impact of BPAR on eGFR over time with imputation. Values missing due to death or graft loss were imputed as zero.

BPAR, biopsy-proven acute rejection; CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate.

