Treatment of De Novo Renal Transplant Recipients With Calcineurin Inhibitor-free, Belatacept Plus Everolimus–based Immunosuppression

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Supplemental material

Table S1. List of Independent Ethics Committees (IEC) and/or Institutional Review Boards (IRB)

Study Site	IEC/IRB Name	IEC/IRB Protocol No.	IEC/IRB Approval No.
University of Virginia	University of Virginia Institutional Review Board for Health Sciences Research	IM10177	17482
California Institute of Renal Research	Sharp Healthcare Institutional Review Board	140598	
Emory University	Emory University IRB	IRB00072295	CR5_IRB0072295
California Pacific Medical Center	Western Institutional Review Board	1156605	20132295
Central PA Transplant Foundation	Pinnacle Health Institutional Review Board	PHH# 14-016	
University of Colorado Hospital Anschutz Medical Campus	Western Institutional Review Board	1146595	20132295
University of Colorado Hospital Anschutz Outpatient Pavilion	Western Institutional Review Board	1142089	20130763
Clinica Privada Velez Sarsfield	Clinica Chutro CIEIS	IM 103177	
Sanatorio Parque S.A.	Comite de Docencia E Investigacion Sanatorio Parque S.A.	IM103177	
University of Illinois at Chicago	University Of Illinois At Chicago, Office for Protection of Research Subjects (OPRS), Office of Vice Chancellor for Research	2014-0405	00006437
Clinica de Nefrologia, Urologia y Enf. Cardiovasculares	Comité de Etica en Investigacion Clinica	IM103177	1105/23/2014
Vanderbilt University Medical Center	Vanderbilt University Medical Center, Human Research Protection Program	140714	
Yale University	Yale University, Human Investigation Committee	1406014090	RNI00000856
Georgetown University Hospital	Georgetown University IRB	2014-0244	

Wake Forest University School of Medicine	Human Research Protection Program IRB, Wake Forest University Health Sciences	IRB00027206	
Inova Fairfax Hospital	Western Institutional Review Board	1159767	20132295
Erie County Medical Center	SUNY Buffalo Health Sciences, Health Sciences IRB		MODCR00001527
Tulane Medical Center	Tulane Human Research Protection Office, Tulane University Biomedical IRB	IM103177	572705
Saint Barnabas Medical Center	Saint Barnabas Medical Center IRB	15-28	7605
Swedish Medical Center, Swedish Organ Transplant and Liver Center	Western Institutional Review Board	1157400	20132295
Presbyterian St. Lukes Medical Center, Colorado Kidney Care	Western Institutional Review Board	1163408	20132295

Table S2. Treatment exposure (mITT analysis)

	BELA+EVL (n = 25)		TAC+MMF (n = 33)	
Treatment duration, days				
Mean (SD)	691.2 (193.8)		652.9 (226.3)	
Median (range)	757.0 (56–765)		737.0 (11–783)	
BELA infusions, n				
Median (range)	29.0 (4–29)		NA	
Daily dose of corticosteroids	**n**	**mean (SD), mg**	**n**	**mean (SD), mg**
Day 1	25	664.0 (137.1)	32	664.5 (153.6)
Day 2	24	340.1 (154.6)	33	313.5 (3.7)
Day 3	25	166.2 (70.4)	30	173.3 (64.4)
Day 4	25	76.7 (50.3)	27	74.9 (30.2)
Day 5	22	39.0 (27.7)	24	33.4 (9.4)
Day 6	19	38.4 (36.3)	22	32.7 (8.2)
Day 7	17	30.2 (6.0)	16	30.5 (1.9)
Daily dose of EVL or MMF	**n**	**mean (SD), mg**	**n**	**mean (SD), mg**
≤1 month	25	3.2 (1.0)	33	1802.0 (398.0)
2–3 months	24	3.4 (1.6)	31	1735.3 (445.3)
4–6 months	23	3.2 (1.7)	30	1647.9 (594.7)
7–9 months	22	3.0 (1.6)	29	1529.9 (632.6)
10–12 months	22	2.8 (1.5)	29	1523.5 (630.1)
13–15 months	22	2.7 (1.5)	28	1536.7 (529.3)
16–18 months	21	2.7 (1.6)	28	1401.4 (565.2)
19–21 months	21	2.7 (1.5)	28	1343.2 (604.9)
22–24 months	21	2.5 (1.4)	27	1342.3 (606.7)

	BELA+EVL (n = 25)		TAC+MMF (n = 33)	
rATG induction dose	**n**	**mean (SD), mg/kg**	**n**	**mean (SD), mg/kg**
Dose 1[a]	25	1.4 (0.3)	33	1.4 (0.2)
Dose 2	25	1.3 (0.3)	32	1.3 (0.2)
Dose 3	25	1.3 (0.3)	31	1.4 (0.5)
Dose 4	11	1.0 (0.1)	11	1.0 (0.2)
Dose 5	5	1.1 (0.2)	2	1.0 (0.0)

[a]Dose1 (baseline/day of transplantation). BELA, belatacept; EVL, everolimus; mITT, modified intent-to-treat; MMF, mycophenolate mofetil; NA, not applicable; rATG, rabbit antithymocyte globulin; TAC, tacrolimus.

Table S3. Serum trough concentrations of BELA, EVL, and TAC

	BELA		EVL		TAC	
	n	mean (SD), μg/mL	n	mean (SD), ng/mL	n	mean (SD), ng/mL
Week 4	22	32.26 (9.25)	23	7.06 (3.46)	32	8.32 (2.47)
Week 12	--	--	19	7.38 (3.04)	30	9.00 (3.19)
Week 20	21	7.72 (3.93)	20	5.58 (2.21)	28	9.72 (4.30)
Week 24	21	5.75 (2.93)	22	6.83 (2.46)	26	8.36 (2.48)
Week 48	--	--	20	5.85 (2.47)	--	--
Week 52	19	5.78 (2.93)	20	4.95 (1.88)	26	7.95 (3.07)
Week 76	--	--	17	4.47 (1.85)	20	7.28 (2.50)
Week 104	--	--	18	5.65 (2.28)	15	7.20 (1.72)

BELA, belatacept; EVL, everolimus; TAC, tacrolimus.

Table S4. Antihypertensive medications and lipid-lowering therapy (ITT analysis)

	BELA+EVL (n = 26)	TAC+MMF (n = 32)
Antihypertensive drug therapy		
Baseline		
Patients who received medications, n	18	21
Number of medications, mean (SD)	2.1 (0.8)	2.3 (1.9)
Month 24		
Patients who received medications, n	18	20
Number of medications, mean (SD)	1.7 (1.0)	1.9 (0.9)
Lipid-lowering drug therapy		
Baseline		
Patients who received medications, n	9	8
Number of medications, mean (SD)	1.2 (0.4)	1.0 (0)
Month 24		
Patients who received medications, n	13	15
Number of medications, mean (SD)	1.5 (0.7)	1.2 (0.4)

BELA, belatacept; EVL, everolimus; ITT, intent-to-treat; MMF, mycophenolate mofetil; TAC, tacrolimus.

Figure S1. Trial design. [a]All doses of rATG were preceded by intravenous methylprednisolone premedication. The first dose of rATG induction was administered intraoperatively prior to vascular reperfusion of the allograft. [b]It was a requirement to test for the presence of anti-BELA antibodies; this was applied only to patients randomized to BELA+EVL who either prematurely discontinued or did not continue to receive BELA following the final week 104 study visit. BELA, belatacept; BPAR, biopsy-proven acute rejection; DSA, donor-specific antibody; eGFR, estimated glomerular filtration rate; EVL, everolimus; MMF, mycophenolate mofetil; rATG, rabbit antithymocyte globulin; TAC, tacrolimus.