Supplementary Table 2. Clinical study schedule: follow-up from 1 week after discharge

Procedure	Follow-up after TP (*continued*)												
	Follow-up after discharge (~12 weeks)[24]				Follow-up after discharge (16 weeks–2 years)[x,z,aa]								
Visit	V17	V18	V19	V20	V21	V22	V23	V24	V25	V26	V27	V28	V29/EOS
Week or year	W2	W4	W8	W12	W16	W24	W32	W40	W52 (1Y)	W64	W76	W88	W104 (2Y)
Window period, wk	±2			±4			±8			±12			±16
Acquire consent form[a]													
Confirm enroll/exclusion													
Demographic information[b]													
Weight/height measurement[c]	√	√	√	√	√	√	√	√	√	√	√	√	√
Vital signs (HR, BP)[d]	√	√	√	√	√	√	√	√	√	√	√	√	√
Basic disease information[e]													
Medical history[f,f1]													
Prior/concomitant medication[g]	√	√	√	√	√	√	√	√	√	√	√	√	√
Physical examination[h]	√	√	√	√	√	√	√	√	√	√	√	√	√
Electrocardiogram (12-lead)						√			√		√		√
Pregnancy test[i]						√			√				√
Laboratory test 1[j]		√		√		√			√		√		√
Laboratory test 2[j]	√		√		√		√	√		√		√	
Blood coagulation test[j]													
Infectious disease test[j,k]													
Oral GTT[l]				√		√			√		√		√
Porcine C-peptide				√		√			√		√		√
HbA1c, FPG		√		√		√			√		√		√
Thyroid function test[m]						√			√				√
Atherosclerosis factors[n]									√				√
Autoantiboies[o]				√		√			√		√		√
Chest X-ray						√			√		√		√
Abdomen ultrasonogram									√				√
Carotid doppler/IMT									√				√
Abdomen CT scan													
Fundus/CPT						√			√		√		√
SMBG[p]							Continuous						
CGMS[q]						√			√		√		√
Hypoglycemia education[q]													
MDI or insulin pump[q]													
Cancer screening (PET, HRCT)													
IP manufacturing (porcine islet isolation)													
IP transplantation													
Assessment of AE/toxicity[r]	√	√	√	√	√	√	√	√	√	√	√	√	√
hCMV, EBV[s]		√	√	√		√			√		√		√
PERV/antiGal Ab/pCMV[t,u]		√	√	√		√			√		√		√
PRA[v]		√				√			√				
Drug blood level[w]	√	√	√	√	√	√	√	√	√	√	√	√	√

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Supplementary Table 2. Continued

Procedure	Follow-up after TP (*continued*)												
	Follow-up after discharge (~12 weeks)[24]				Follow-up after discharge (16 weeks–2 years)[x,z,aa]								
Visit	V17	V18	V19	V20	V21	V22	V23	V24	V25	V26	V27	V28	V29/EOS
Week or year	W2	W4	W8	W12	W16	W24	W32	W40	W52 (1Y)	W64	W76	W88	W104 (2Y)
Window period, wk	±2		±4		±8				±12				±16
Consult to Division of Infectious Disease													
Consult to Neuropsychiatry													
Confirm COVID-19 vaccine[x]													
COVID-19 PCR test[x]													
Infection prevention	Conduct according to corresponding drug administration schedule									Not applicable			
Immunosuppresion[y]	Administer according to corresponding drug administration schedule below												

TP, transplantation; EOS, end of study; HR, heart rate; BP, blood pressure; GTT, glucose tolerace test; HbA1c, glycosylated hemoglobin; FPG, fasting plasma glucose; IMT, intima-media thickness; CT, computed tomography; CPT, Current Procedural Terminology; SMBG, self-monitoring of blood glucose; CGMS, continuous glucose monitoring system; MDI, multiple daily injection; PET, positron emission tomography; HRCT, high resolution computed tomography; IP, investigational product; AE, adverse effect; hCMV, human cytomegalovirus; EBV, Epstein-Barr virus; PERV, porcine endogenous retrovirus; antiGal Ab, anti-Galα1-3Galβ1-4GlcNAc-R antibody; pCMV, porcine cytomegalovirus; PRA, panel reactive antibody; COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction.

[a]Must be obtain written consent before and after active intervention (V1 and V6): [a1]Before active intervention (visit 1) (using written consent for before active intervention), [a2]After active intervention for 6 months (V1–V6) (visit 6) (using written consent for after active intervention).

[b]Demographic information: date of birth, age, and gender (V1) is collected.

[c]Weight/Height measurements: Weight is measured. But during visit 1 and visit 7, height and weight are measured.

[d]Vital signs: Vital signs, including systolic and diastolic blood pressure, and heart rate are measured.

[e]Basic disease information: Date of diagnosis for type 1 diabetes mellitus is checked.

[f]Medical history: Medical history within 24 weeks before the screening (hypoglycemia within 1 year, malignant tumor within 5 years, liver cirrhosis during lifetime) are checked. Clinically significant or abnormal medical conditions observed before porcine islet xenotransplantation are considered medical history: [f1]Checked any history of hypoglycemia within the past 6 months.

[g]Prior/concomitant medication: Prior medication administered within 4 weeks of screening and concomitant medications after acquiring a written consent are checked.

[h]Physical examination: Clinically significant abnormal results before porcine islet transplantation are recorded on the medical history and the clinically significant abnormal results after porcine islet transplantation is recorded on AE.

[i]Pregnancy test: Urine test (urine-human chorionic gonadotropin) is done to check for pregnancy in women with childbearing potential.

[j]Laboratory test: If there is a test result within 2 weeks, visit 1 test can be replaced with that result based on investigator's discretion.

Classification	Visit		Detailed category
Laboratory test 1	Visit 1 (screening), Visit 7, Visit 18, Visit 20, Visit 22, Visit 25, Visit 29 (EOS)	Hematologic test	Hematocrit, hemoglobin, MCV, MCH, MCHC, RBC, WBC, platelet, basophil, eosinophil, neutrophil, lymphocyte, monocyte, ESR
		Blood chemistry	ALT, AST, ALP, glucose, BUN, creatinine, total cholesterol, total bilirubin/direct bilirubin, CPK, LDH, uric acid, total protein, albumin, sodium, potassium, chloride, calcium, phosphorus, magnesium, LDL, HDL, TG, r-GTP, CRP, C-peptide (However, the C-peptide test is conducted on Visit 1 only.)
		Urinalysis and urine chemistry	Color, specific gravity, pH, leucocytes, nitrite, protein, glucose, ketone, urobilinogen, bilirubin, RBC, Microscopy, 24 hr urine chemistry (microalbumin, protein, creatinine, calcium, phosphorus, sodium, potassium, urea, osmolarity)
Laboratory test 2	Visit 9–Visit 17, Visit 19, Visit 21, Visit 23, Visit 24, Visit 26, Visit 28	Hematologic test	Hematocrit, hemoglobin, MCV, MCH, MCHC, RBC, WBC, platelet, basophil, eosinophil, neutrophil, lymphocyte, monocyte, ESR
		Blood chemistry	ALT, AST, ALP, glucose, BUN, creatinine, total bilirubin/direct bilirubin, total protein, albumin, sodium, potassium, calcium, phosphorus
Blood coagulation test	Visit 7, Visit 13	Blood coagulation test	PT, aPTT, BT/CT
Infectious disease test	Visit 1, Visit 7	Serologic test	HAV Ab (IgG), HBsAg, HBsAb, HBeAg, HBeAb, HBcAb (IgG), HCV Ab, HIV Ag, HIV Ab, HTLV Ab, Herpes (IgG), hCMV (IgM/IgG), EBV (EBNA IgM/IgG), VDRL (syphilis, qualitative), IGRA (tuberculosis), Toxoplasma (parasite, IgG)
Viral disease test	Visit 7, Visit 16, Visit 18–20, Visit 22, Visit 25, Visit 27, Visit 29	Virus test	Human: Human CMV (hCMV, quantitative PCR), human EBV (quantitative PCR) Pig: PERV, porcine CMV (pCMV), PCV3, HEV, Swine influenza

[k]Prior to administering immunosuppressive drugs, tests for infectious diseases such as hepatitis A virus (HAV) Ab (immunoglobulin G [IgG]), venereal disease

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Supplementary Table 2. Continued

research laboratory (VDRL) (syphilis, qualitative), tuberculosis (X-ray, chest CT, interferon-gamma releasing assay [IGRA]), and infectious disease tests such as hepatitis, toxoplasma (parasites, IgG), and AIDS are performed.

[l]Oral glucose tolerance test (OGTT): 75 g oral OGTT is performed to measure insulin, C-peptide and glucose at visit 7, visit 16, visit 20, visit 22, visit 25, visit 27 & visit 29

[m]Thyroid function test: Thyroid-stimulating hormone and free thyroxine are measured. If there is a test result within 2 weeks, visit 1 test can be replaced with that result based on investigator's discretion.

[n]Atherosclerosis factors: Apo(a), apo(b), plasminogen, von Willebrand's factor Ag, lipoprotein A, fibrinogen, plasminogen activator inhibitor-I, homocysteine and free fatty acid are measured. If there is a test result within 2 weeks, visit 1 test can be replaced with that result based on investigator's discretion.

[o]Auto-antibody test: Anti-insulinoma-associated protein 2 (IA2) Ab and anti-glutamic acid decarboxylase Ab are tested. If there is a test result within 2 weeks, visit 1 test can be replaced with that result based on investigator's discretion.

[p]SMBG: The subject self-measures blood glucose peripherally seven times (before/after each meal and before going to bed) 1 day before V1–V16, and every visit after discharge (V17–V29). SMBG data recorded before transplant (V1) to a day before 104 weeks after transplant (V29) is collected as much as possible. (After obtaining consent, the patient measures SMBG three to four times a day, excluding the day of transplantation [V12], and checks their records at each visit.)

[q]After obtaining written consent active intervention is performed using daily glucose measurement and regular education for 6 months (24 weeks) (V1–V6). When necessary, intervention is performed using CGMS and insulin pumps. (If possible, results of CGMS [esp. time below target range] are compared).

[r]For toxic response assessment, the presence of toxic response and severity are assessed according to World Health Organization standards.

[s]Before and after administering immunosuppressive drugs, hCMV (hCMV quantitative PCR) and EBV (EBV quantitative PCR) tests are performed at regular intervals along with a confirmation of systemic symptoms. If infection is suspected (such as fever), tests are performed more frequently, appropriate antiviral agents are administered after consultation with Division of Infectious Disease.

[t]Real-time PCR tests for pig-derived viruses (PERV, pCMV, porcine circovirus type 3 [PCV3], hepatitis E virus [HEV], Swine influenza) are performed at regular intervals, and the tests are performed at the Department of Diagnostic Laboratory Medicine at Gachon University Gil Hospital (or Clinical Trial Research Laboratory). In cases where infection is suspected due to the use of immunosuppressive agents, inflammatory markers (erythrocyte sedimentation rate [ESR], high-sensitivity C-reactive protein [hsCRP], procalcitonin, etc.) and blood coagulation (prothrombin time [PT], activated partial thromboplastin time [aPTT], bleeding time and clotting time [BT/CT]) are checked, and appropriate medications are used after consultation to the Division of Infectious Disease.

[u]If there is suspicion of worsening of a sudden systemic illness, abnormal blood clotting, and cytokine storm, the patient can be isolated in the Intensive Care Unit where antibiotic treatment and life-sustaining therapies (extracorporeal membrane oxygenation, mechanical ventilation, dialysis, etc.) may be provided. Laboratory tests for various cytokines (tumor necrosis factor-α, interleukin [IL]-1β, IL-6) can be performed experimentally. If the patient develops a fever, tests for major infectious agents in allogeneic transplantation, such as hCMV (hCMV quantitative PCR), EBV (EBV quantitative PCR), and toxoplasma (parasite, IgG), can be conducted, and if excluded, real-time PCR testing for porcine related viruses (PCMV, porcine adenovirus, porcine lymphotropic herpesvirus [PLHV]-1,2, pseudorabies, PCV-1,2,3) identified by Whole Genome Sequencing (WGS) of the original pig islet can be performed to identify the exact cause of infection.

[v]PRA tests are conducted before transplantation (visit 1) and after transplantation (visit 18, visit 22, visit 25).

[w]Drug concentration: The blood concentration of immunosuppressants is measured, and the collection time is determined according to the type of immunosuppressant. The frequency of measurements can be adjusted based on the researcher's judgment.

[x]After obtaining consent, the COVID-19 vaccination status is checked between visit 1 and visit 6, and if the patient is not vaccinated, vaccination can be administered. Upon admission (visit 7), PCR antigen testing is performed.

[y]Systemic immunosuppressants: Administration of immunosuppressants follows the 'Immunosuppressant Schedule.' The dosage can be adjusted based on the patient's condition under the researcher's judgment, and another immunosuppressant used in transplantation can be administered based on the researcher's judgment depending on the status of the rejection reaction.

[z]The length of hospital stay after transplantation can be extended based on the researcher's judgment depending on the patient's condition.

[aa]Research subjects who drop out early must perform the tests planned for EOS (visit 29) through termination visit.