CellTrans
PIONEERING CELL THERAPIES™

Administration of Donislecel-jujn (Lantidra™)

Center for Medicare & Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting

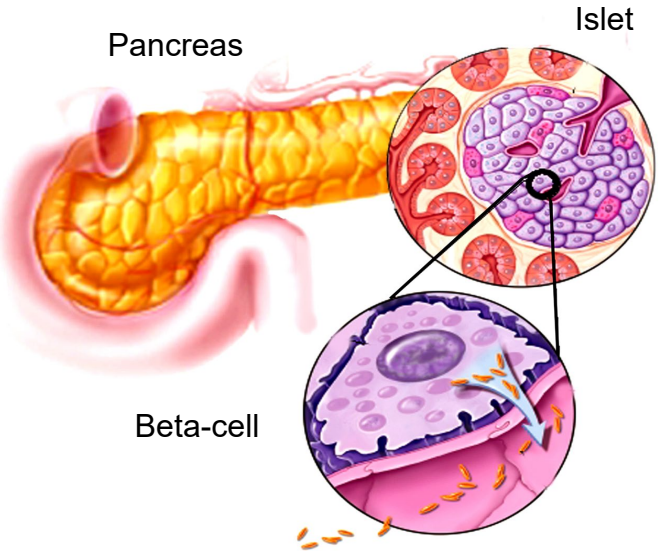
March 19-20, 2024

Unmet Need for Type 1 Diabetics Unable to Achieve Target HbA1c

- Type 1 diabetes (T1D): autoimmune disease involving loss of insulin-producing beta cells within pancreatic islets of Langerhans. Insulin is the hormone which controls blood sugar levels. 1.4+ million impacted in the US.[1]

- A subset of patients experience “hard-to-control” T1D, a serious condition in which a person's blood sugar level frequently and unpredictably moves from low to high and high to low. They suffer from hypoglycemia unawareness and severe hypoglycemia.

- Lantidra™ Indication: adults with T1D who are unable to approach target hemoglobin A1c (HbA1c) because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education (i.e. exogenous insulin injections, continuous glucose monitors (CGMs), insulin pumps).



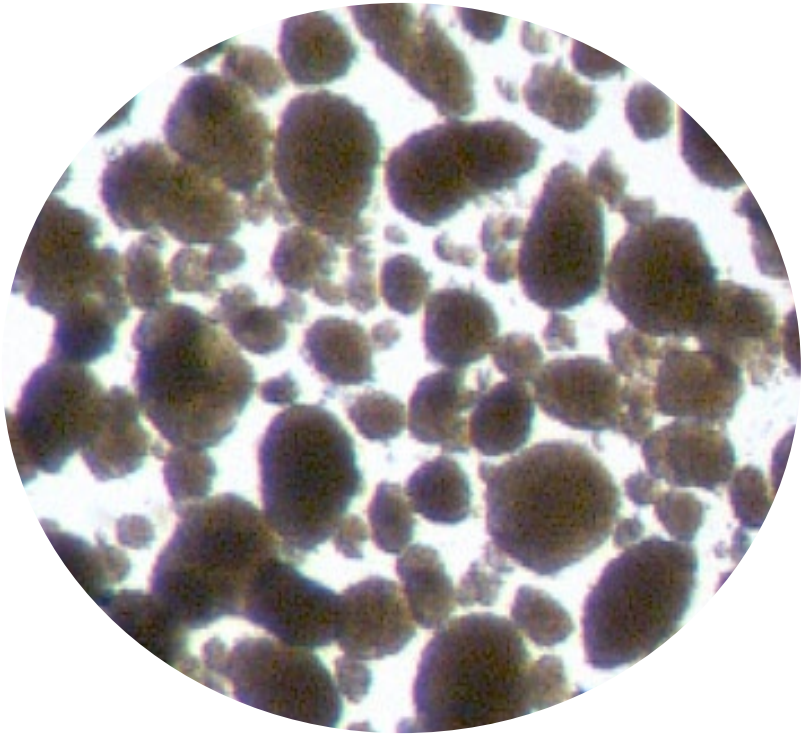
Insulin secretion into the bloodstream

[Image Credit: © 2001 Terese Winslow (assisted by Lydia Kibiuk)]

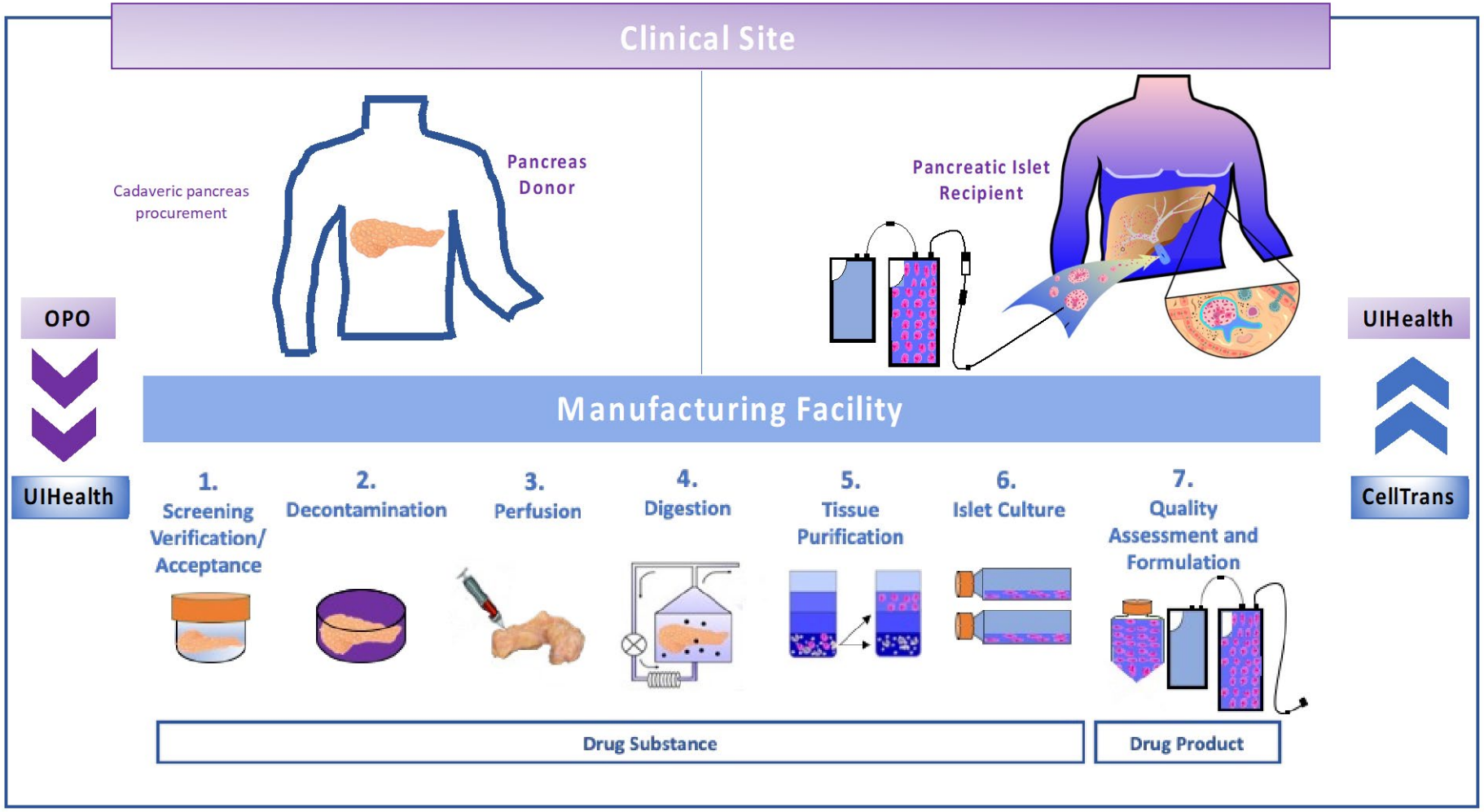
1. Centers for Disease Control and Prevention, *National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States*, U.S. Department of Health and Human Services, Editor. 2020: Atlanta, GA, USA.

Lantidra™: First FDA-Approved, Cellular Therapy to Treat T1D

- FDA approved the Biologic License Application (BLA) for Lantidra™ on June 28, 2023.
- United States Adopted Name (USAN): Donislecel-jujn (Allogeneic Pancreatic Islet Cellular Suspension for Hepatic (Liver) Portal Vein Infusion).
- Product Description: a cellular suspension (light yellow liquid with the presence of visible cellular aggregates) of allogeneic pancreatic islets (islets of Langerhans), from the pancreas of a single deceased donor, in buffered transplant media containing sodium chloride, dextrose, minerals, amino acids, vitamins, and other compounds supplemented with HEPES (2-[4-(2-hydroxyethyl)piperazin-1-yl] ethanesulfonic acid; 10 mM final concentration) and human serum albumin (0.5% final concentration).
- Mechanism of Action: secretion of insulin by the beta cells within the infused allogeneic islet of Langerhans. Functionally, islets of Langerhans are responsible for regulating blood glucose levels in response to glucose stimulation.

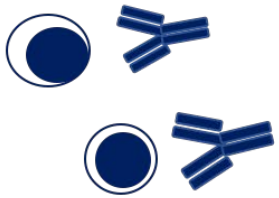


Lantidra™ Manufacturing Process: High Quality Islets Produced in a GMP Facility



Post-Manufacturing of Lantidra™: Patient Sequence of Events

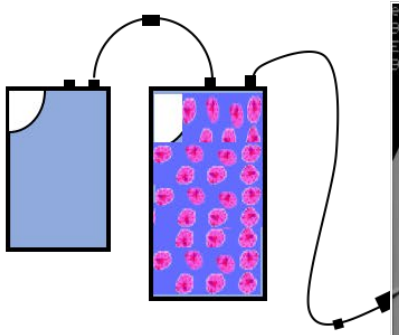
- ☑ Release Criteria
- ☑ Donor-recipient Cross Matching
- Recipient selection based on:
  - ☑ Cross-match and UNOS Organ Allocation Rules
  - ☑ IEQ/kg Requirement

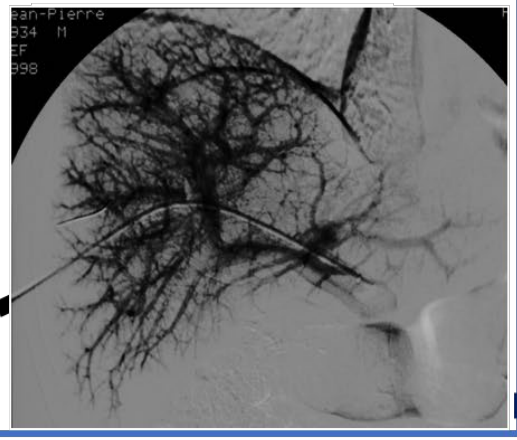


- ☑ Hospital Admission of best matched waitlisted patient

- ☑ Admission exams
- ☑ Induction Immunosuppression & Anti-infectious Prophylaxis

- ☑ Radiology Suite & Portal Catheter Placement
- ☑ Donislecel infused via the portal vein



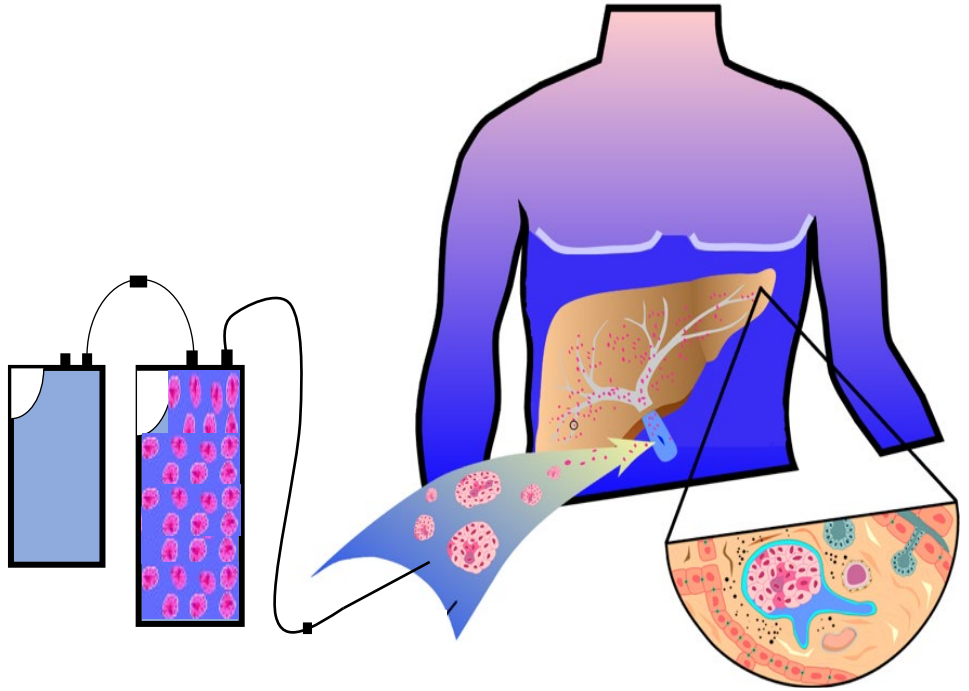


- ☑ Catheter Withdrawn Under Ultrasound or Fluoroscopic Guidance
- ☑ Intrahepatic Track Embolized with Hemostatic Agent
- ☑ Ultrasound Exam to Rule Out Bleeding from Liver Surface

Administration of Lantidra™: Infusion into Hepatic (Liver) Portal Vein

- Administration of Lantidra™ is minimally invasive and presents a safer alternative to whole pancreas transplantation. Used in conjunction with immunosuppression.

- Interventional radiologists and surgeons with expertise in islet cell infusion may administer Lantidra™ in an interventional radiology suite or operating suite under controlled aseptic conditions (i.e., inpatient setting). Patients are monitored in hospital for a minimum of 24 hours post procedure.



- Infusion of Lantidra™ may be performed using a percutaneous or laparoscopic approach. An open approach may be utilized if deemed necessary by the surgeon.

Lantidra™ Administration Procedure: Infusion into Hepatic Portal Vein

- **Lantidra™ Infusion & Monitoring During Procedure**

1. Apply local anesthesia at infusion site identified by ultrasound, access a peripheral portal vein branch with a fine needle, and confirm intraportal location (in liver) with contrast. Pass guidewire into main portal vein and insert catheter into portal vein.

2. Once the catheter placement in the portal vein is confirmed, connect the intravenous tubing from the LANTIDRA™ infusion bag to the catheter using a Luer lock connector.

3. Infuse all infusion bags by gravity flow over approximately 30 minutes at rates ≤ 25 mL/kg/h. Flush the infusion lines periodically to clear them.

4. Measure portal pressure during the infusion. Pause infusion if portal pressure rises above 22 mmHg and do not resume until it falls below 18 mmHg. Terminate infusion if portal pressure remains above 22 mmHg for longer than 10 minutes.

5. Monitor blood glucose levels every 15 minutes during the infusion and then every 30 minutes for the first 4 to 8 hours after infusion. Provide appropriate treatment if blood glucose levels fall below 70 mg/dL.

- **Lantidra™ Package Insert Contains Additional Information**

Lantidra™: Dosage and Number of Administrations

- Each infusion (i.e. administration) uses one lot of Lantidra™, which consists of islets manufactured from the pancreas of a single deceased donor.

- Patients receive a minimum of 1 infusion and a max of 3 infusions. A second infusion may be performed if the patient does not achieve independence from exogenous insulin within one year of infusion or within one year after losing independence from exogenous insulin after a previous infusion. A third infusion may be performed using the same criteria as for the second infusion.

- Lantidra™ dose = **Islet Equivalents (IE)** per kilogram of recipient's body weight (IE/kg)
  - Recommended dosage: ≥5,000 IE/kg for initial transplant; ≥4,500 IE/kg for subsequent transplants

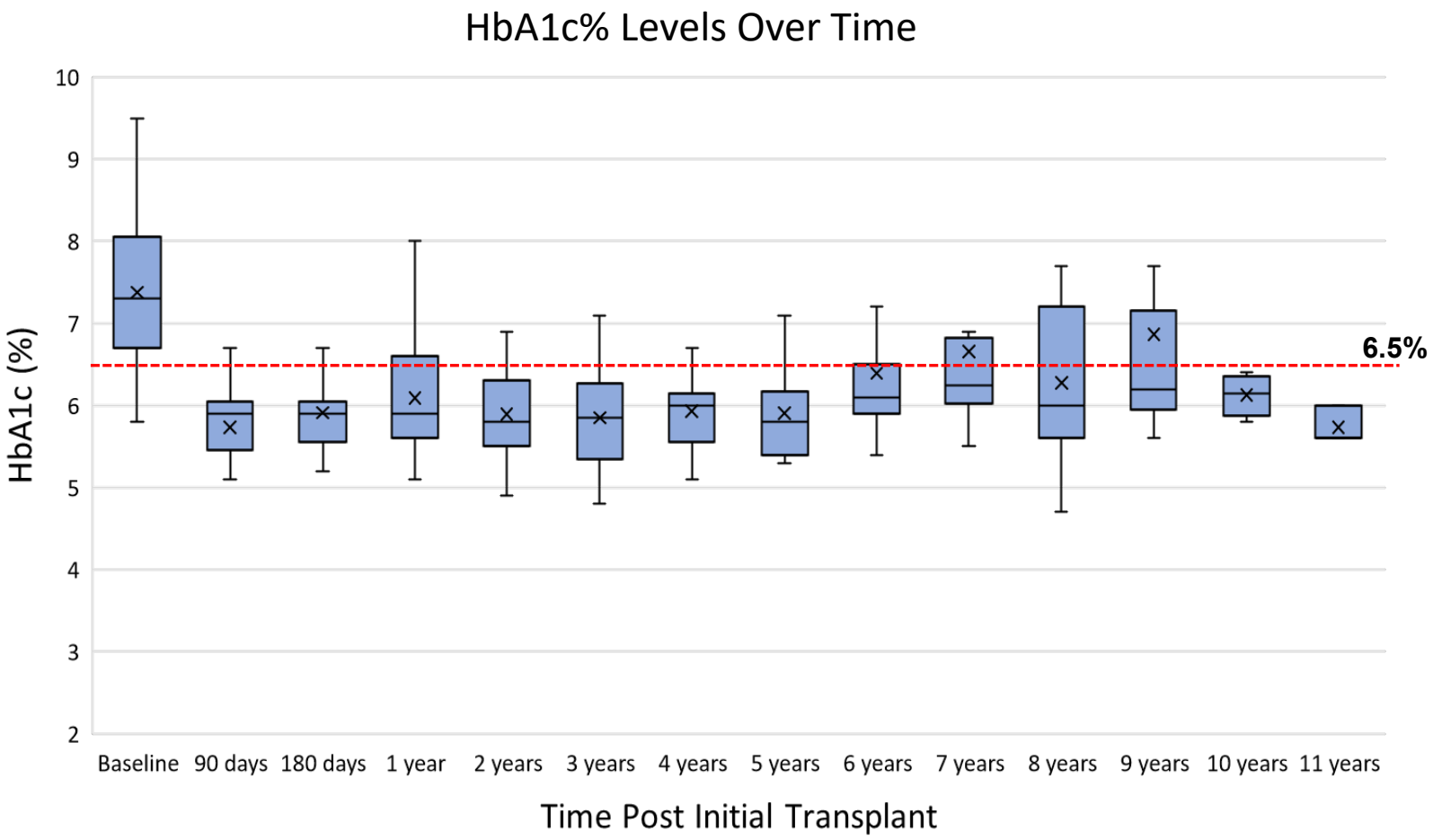
- Each dose of Lantidra™ is provided as two (2) infusion bags connected to each other via sterile connector.
  - One bag contains Lantidra™ up to a maximum of 1 x 10^6 EIN in 400mL of transplant media and the second bag (Rinse Bag) contains transplant media (light yellow liquid only with no cellular aggregates present) used to rinse the Lantidra™ bag and the infusion line.

Lantidra™: Documentation of Administration

- Documentation of administration within the medical record would most commonly be found in the physician procedure report and progress notes.

Long-Term Glycemic Control Achieved Post-Administration of Lantidra™

- UIH-001 (Study 1) and UIH-002 (Study 2); Pooled Population (n=30)
- After the administration of Lantidra™ the median HbA1c% remains below the target of ≤6.5% throughout long-term follow up
- Additional efficacy data available in FDA Advisory Committee Briefing Packet



Lantidra™ Safety Profile

- Safety has been examined in 2 core studies (UIH-001 and UIH-002; Pooled Population; N=30).
- Lantidra™ demonstrated a safety profile consistent with known risks of the transplant procedure and concomitant medication use, especially long-term use of immunosuppressants.
- For the Pooled Population from initial transplant through 1 year after last transplant:
  - Treatment-emergent adverse events (TEAEs) occurred in all patients, regardless of the number of transplants.
  - There were no TEAEs leading to early discontinuation
  - There were no TEAEs leading to death
  - Approximately 53% of patients experienced a serious adverse event (SAE, ~3% of all TEAEs)
  - Approximately 83% of patients experienced a TEAE of Grade 3 or higher (~13% of all TEAEs)
  - Approximately one quarter of all TEAEs reported during primary follow-up occurred within the first week post-transplant, and approximately one half occurred within the first month.

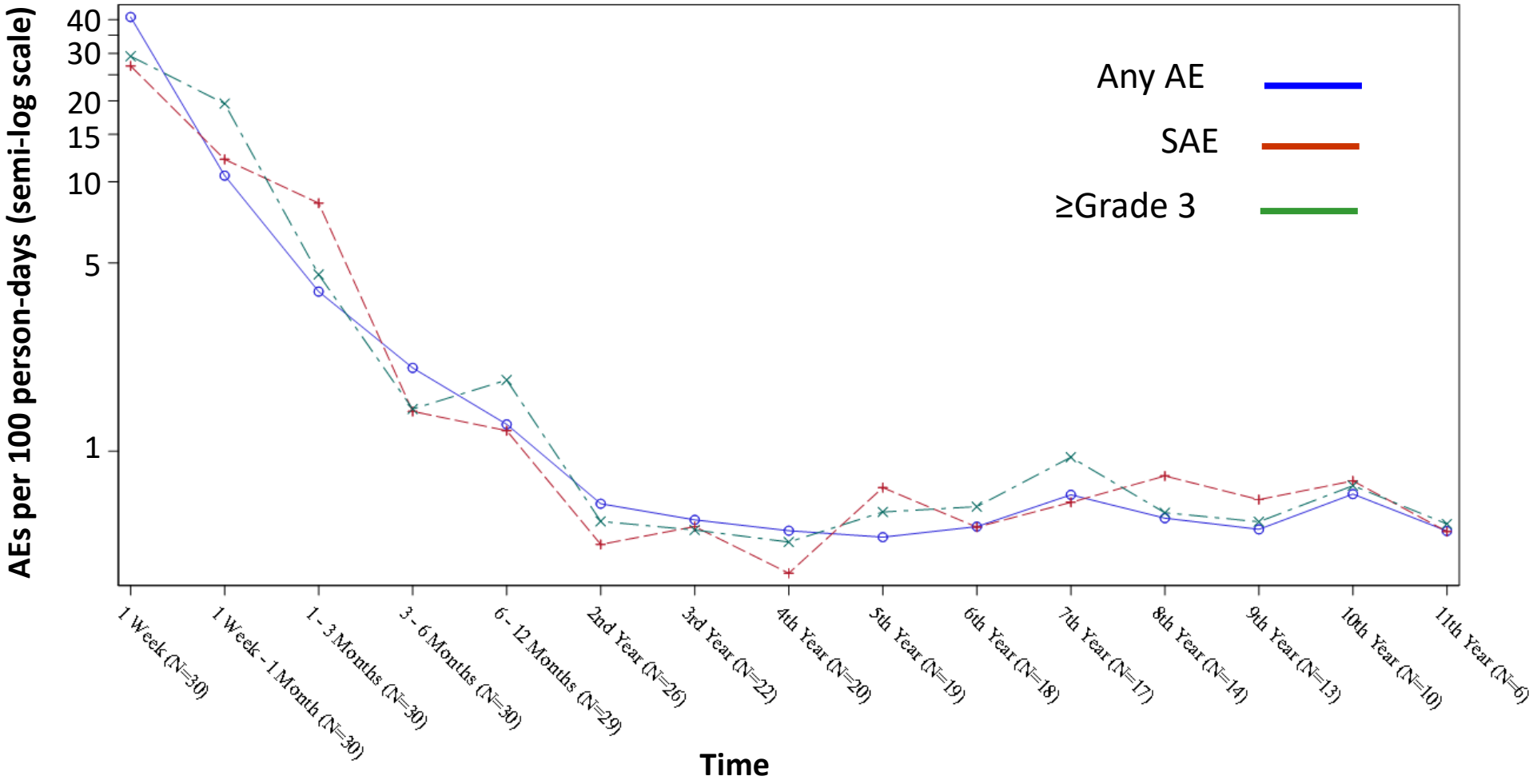
Most Common Treatment Emergent Adverse Events (TEAEs)

TEAEs Occurring in ≥50% of Patients through 1 Year after Last Transplant (Pooled Population)

Preferred Term	Patients (N=30) n (%)	
	Any Grade	≥Grade 3
Acne	26 (87)	2 (7)
Anemia	25 (83)	6 (20)
Nausea	25 (83)	6 (20)
Fatigue	24 (80)	3 (10)
Diarrhea	22 (73)	7 (23)
Abnormal loss of weight	22 (73)	2 (7)
Transaminases increased	19 (63)	2 (7)
Headache	19 (63)	3 (10)

Preferred Term	Any Grade	≥Grade 3
Vomiting	18 (60)	4 (13)
Abdominal pain	17 (57)	5 (17)
Asthenia	17 (57)	2 (7)
Hyponatremia	16 (53)	3 (10)
Oropharyngeal pain	16 (53)	2 (7)
Pruritus	16 (53)	0
Dizziness	15 (50)	2 (7)

Treatment Emergent Adverse Events Over Time



Most Common Serious Adverse Events (SAEs)

SAEs Occurring in ≥5% of Patients through 1 Year after Last Transplant (Pooled Population)

Through 1 Year after Last Transplant

Preferred Term	Events n (%)	Patients (N=30) n (%)
Any SAE	**37 (100)**	**16 (53.0)**
Anemia	3 (8.1)	3 (10.0)
Pneumonia	3 (8.1)	3 (10.0)
Nausea	2 (5.4)	2 (6.7)

Beyond 1 Year after Last Transplant

Preferred Term	Events n (%)	Patients (N=26) n (%)
Any SAE	42 (100)	17 (65.4)
Hyponatremia	4 (9.5)	2 (7.7)
Basal Cell Carcinoma	2 (4.8)	2 (7.7)
Myocardial Ischemia	2 (4.8)	2 (7.7)
Squamous Cell Carcinoma of Skin	2 (4.8)	2 (7.7)
Syncope	2 (4.8)	2 (7.7)

Naming Conventions

- Proprietary Name: LANTIDRA™
- USAN: Donislecel-jujn
- Allogeneic Pancreatic Islet Cellular Suspension for hepatic portal vein infusion

Summary: Lantidra™ Safety Profile

- TEAEs were more frequent within 1 year of transplant.
  - Most frequent within first week, declining to a low level by end of first year

  Remained low through long-term follow-up

- Most side effects were considered related to immunosuppression

- No procedure-related deaths occurred

- Additional safety data available in FDA Advisory Committee Briefing Packet

Summary: Lantidra™ is a Safe, Efficacious Treatment & Improves Quality of Life for T1D Patients

- For patients suffering from ”hard to control” T1D, Lantidra™ fills a significant medical need, is effective at restoring good glycemic control in most patients, improves patient quality of life, and poses an acceptable safety risk.

- The Lantidra™ administration procedure is minimally invasive, safe, and includes less procedural risk than whole pancreas transplantation.

- The primary risk from Lantidra™ is related to concomitant medications, particularly immunosuppressants.

- The side effects associated with a steroid-free immunosuppression regimen are expected, although with education of transplant recipients and close follow-up, most adverse events (AEs) can be treated and made self-limiting.[1]

[1] Hafiz, M.M., et al., *Immunosuppression and procedure-related complications in 26 patients with type 1 diabetes mellitus receiving allogeneic islet cell transplantation.* Transplantation, 2005. **80**(12): p. 1718-28.