SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Ex Vivo Lung Perfusion System

Device Trade Name: LungFX™ device

Device Procode: PHO

Applicant's Name and Address: Lung Bioengineering Inc., LB1 Building 1015 Spring Street, Silver Spring, MD 20910

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P240033

Date of FDA Notice of Approval:

Priority Review: None

II. INDICATIONS FOR USE

The LungFX™ device ("LungFX") is indicated for centralized, *ex vivo* (outside the body) evaluation of deceased-donor lungs (single and double) that cannot be placed for transplantation by an Organ Procurement Organization (OPO) with any of the matched candidates if using direct-to-recipient procurement and preservation procedures. LungFX provides normothermic perfusion and ventilation of procured donor lungs initially stored with cold static preservation solution.

LungFX is intended to allow for re-assessment, in a controlled environment, of procured donor lungs' suitability for transplantation into male and female patients aged 18 years or older with end-stage lung disease awaiting first time (double or single) lung transplantation. Lungs accepted for transplantation after LungFX require a second period of storage with cold static preservation solution, and cumulative preservation time of transplanted lungs is not intended to exceed 20 hours.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

A. Warnings

- The LungFX device is not intended for the preservation of donor lungs that could be matched and successfully placed by an OPO without utilization of the device. In the CLES Pivotal Study, the observed 12-month survival rate among recipients of LungFX lungs did not meet the pre-specified performance goal (> 95% posterior probability of 1 year survival > 81.2%); rates of 12-month overall mortality and Clinical Events Committee (CEC)-adjudicated lung graft-related mortality were higher in EVLP subjects as compared to non-EVLP contemporaneous control subjects; and two-year survival within several pre-specified subgroups were clinically less favorable among EVLP donor lungs than among non-EVLP control donor lungs. Before deciding to proceed with LungFX organ preservation, a physician should fully consider the risks and benefits of this device and those of other organ preservation modalities. Transplant physicians are advised to carefully review the available clinical data in the LungFX device labeling when considering its use for any donor lungs and recipients. Refer to section G. Safety and Effectiveness Results for a summary.

- Only qualified Lung Bioengineering (LBE) personnel can operate the LungFX device.

- Only trained physicians can evaluate lung suitability for transplantation after LungFX evaluation.

B. Precautions

- Safety and effectiveness of the LungFX device are derived principally (i.) from clinical data collected prospectively in the CLES Pivotal Study within 1 year after organ preservation and transplantation and (ii.) from 2 years of observational, post-transplantation survival data. Therefore, the impact of the LungFX device on clinical outcomes such as longer-term recipient survival and graft function (e.g., chronic lung allograft dysfunction (CLAD)) is uncertain. Other approved devices allow for pre-transplant assessment of procured donor lungs under conditions of *ex vivo* normothermic perfusion and ventilation, and there are various approaches available for isolated cold static storage preservation of procured donor lungs. Each alternative has its own advantages and disadvantages. A physician should fully discuss these alternatives with transplant candidates to identify the type of donor organ and preservation method that best meet patient expectations.

- Safety and effectiveness of the LungFX device has not been studied in:
  - Patients under the age of 18 years.
  - Patients listed for same-side lung re-transplantation.
  - Patients listed for multiple organ transplantation including lung and any other organ.
  - Patients listed for live donor lobar lung transplant.
  - Patients positive for human immunodeficiency virus (HIV) or *Burkholderia cenocepacia* infection.

- Safety and effectiveness of the LungFX device has not been studied for donors or donor lungs with the following:
  - Confirmed pneumonia and/or persistent purulent secretions identified via bronchoscopy prior to donor lung excision.
  - Confirmed evidence of aspiration.
  - Significant mechanical lung injury or trauma.
  - HIV or active hepatitis C.

- A device malfunction or User error could lead to a potential loss of a donor lung.

Additional warnings and precautions can be found in the LungFX™ device labeling.

V. DEVICE DESCRIPTION

The LungFX is an ex vivo lung perfusion (EVLP) device that uses an acellular perfusate to perfuse the lung to simulate normothermic (37°C) in situ lung function in an ex vivo controlled environment for the purpose of extended preservation and evaluation of potential donor lungs that would not otherwise be used for transplant. LungFX is an assembly of device components comprising a combination of off-the-shelf medical equipment and single-use disposables. The device components fall into 2 classifications: 1) Hardware and 2) EVLP Circuit Single-Use Disposables. A photograph of the device is provided in Figure 1 below.

- The Hardware includes an extracorporeal heater-cooler unit (HCU), intensive care unit (ICU) ventilator, arterial blood gas (ABG) analyzer, and a modular perfusion system comprised of the following: a central workstation with the user interface, a pump console module (inclusive of metal frame, power supply, roller pump, and console/control module), a centrifugal pump driver, and diagnostic module that works with accessory components (flow sensor and temperature probe) and ancillary component (pressure transducers) to

measure and monitor flow, temperature, and pressure. Table 1 below provides a list of operational use parameters for the hardware.

- The EVLP Circuit Single-Use Disposables include an organ chamber, cannula set, perfusate solution, heat exchanger, centrifugal pump head and a perfusion circuit kit consisting of tubing lines, a sample manifold, waste/drain bags, hardshell reservoir, oxygenator, and leukocyte reduction filter. The organ chamber, cannula set, heat exchanger, centrifugal pump head, and perfusion circuit kit are assembled together to form the perfusate loop of the LungFX EVLP circuit. The LungFX EVLP circuit includes the perfusate loop, HCU, perfusion system, and ICU ventilator. The lung in the organ chamber is directly connected to the ICU ventilator and cannula set. The ABG analyzer is a stand-alone component used to analyze perfusate samples taken during an EVLP procedure. A schematic of the EVLP circuit is provided in Figure 1.

The LungFX Hardware and EVLP Circuit Single-Use Disposables are either 510(k)-cleared or PMA-approved by the FDA for human use. These device components are manufactured by their respective firms and intended to be used off-the-shelf. The PMA-approved single-use disposable components are specifically intended for use to perform EVLP. The 510(k)-cleared hardware and single-use disposables were originally intended for use to support extracorporeal bypass perfusion and oxygenation of blood for a living patient during cardiopulmonary surgery. The inclusion of these device components as part of the LungFX device involves no manipulation of the original device components for the LungFX device design or the manufacturing process. Their function in the LungFX device is essentially the same, except acellular perfusate is being circulated instead of blood, the perfusate is deoxygenated to allow oxygenation by the organ, and the devices are being used ex vivo with isolated lungs instead of direct contact with a patient. Where the use of the LungFX Hardware and EVLP Circuit Single-Use Disposable device components to perform EVLP differs from the original intended use (eg, use with perfusate instead of blood), the qualification for use of the hardware and/or single-use disposable component has been performed.

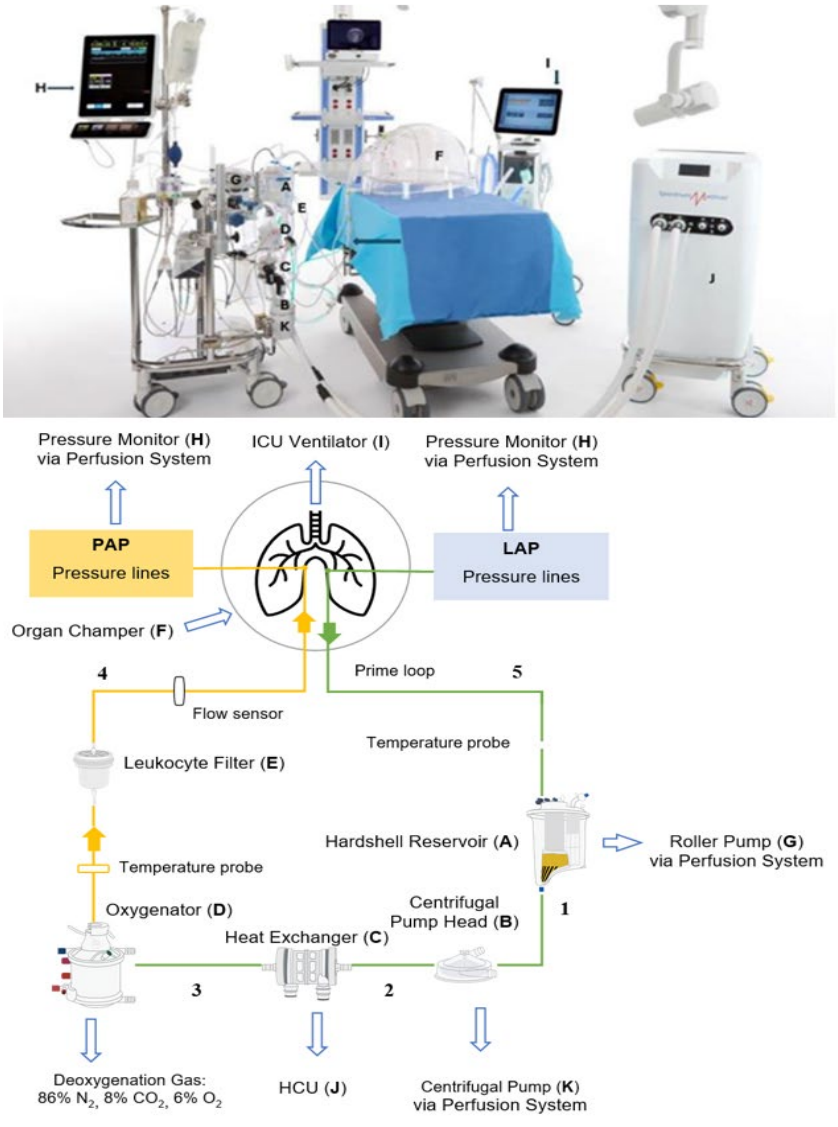
LungFX is intended to be operated/used exclusively by the company, Lung Bioengineering Inc. (LBE), in company-controlled facilities by specifically trained and qualified personnel. LungFX is not to be sold to any other entity nor operated/used by an entity that is not a company-controlled facility.

Table 1: LungFX Preset Limit or Alarm Ranges and Operational Use Parameters

Equipment	**Parameter/ Use**	**Operational Use Parameters**	**Limit or Alarm Ranges**
HCU	Temperature (°C)	4 to 40	
ICU Ventilator: Volume Control	Ppeak (cmH_2O)	0 to 25	Upper limit 25
	Respiratory Rate (b/min)	7 and 10	
	End Expiratory Pressure (cmH_2O)	2 to 10	
	VT (mL)	100 to 2,000*	
	PEEP (cmH_2O)	5	
	FiO2 (%)	21 and 100	

Equipment	Parameter/ Use	Operational Use Parameters	Limit or Alarm Ranges
	I:E ratio	1:2	
	Tpause Time (%):	0	
	Inspiratory Rise Time (%)	5	
	Trigger Pressure	-2	
Perfusion System	Roller Pump Speed (RPM)	0 to 250	
	LA/PA Pressure Monitoring (mmHg)	-10 to 50	2 to 6
	Perfusate Temperature Monitoring (°C)	9 to 39	9.8 to 37.4
	Centrifugal Pump Speed (RPM)	0 to 3,500	
	Flow Rate (LPM)	0 to 10	
ABG Analyzer	Measures PO_2, PCO_2, PH, glucose and lactate	Samples in acellular perfusate	

Abbreviations: EVLP, *ex vivo* lung perfusion; FiO_2, fraction of inspired oxygen; HCU, Heater-Cooler Unit; IBW, Ideal Body Weight; ICU, Intensive Care Unit; I:E, inspiratory :expiratory; LAP, left atrial pressure; LPM, liters per minute; PA, pulmonary artery; Ppeak, Peak Airway Pressure; PEEP, Positive End-Expiratory Pressure; RPM, revolutions per minute; VT, Tidal Volume
*A low and max VT is listed, but during EVLP, the calculation for VT is based on the following: Double Lung VT Maintenance is seven (7) mL/kg x IBW, Double Lung VT O_2 Challenge is 10 mL/kg x IBW; Single Right Lung VT is 60% of Double VT; Single Left Lung VT is 40% of Double VT.



Abbreviations: EVLP, ex-vivo lung perfusion; HCU, heater-cooler unit; ICU, intensive care unit; LAP, left atrial pressure; PAP, pulmonary artery pressure

Figure 1: Schematic of the LungFX Device with EVLP Circuit Flow

The LungFX Device EVLP circuit flow (corresponding to 1-5 as shown in Figure 1 above) is summarized as follows:

1. The perfusate is added into the EVLP circuit through a standard aseptic interface on the hardshell reservoir. The height of the reservoir is adjusted as needed during the EVLP procedure to maintain left atrial (LA) pressure (LAP).

2. The centrifugal pump draws perfusate from the reservoir through the pump head and circulates it through a heat exchanger where the temperature is controlled via the extracorporeal Heater-Cooler Unit.

a. At the start of an EVLP procedure, perfusate is gradually heated to warm the donor lung from cold storage temperatures to normothermic temperatures of ~37°C. During the procedure, the temperature of the perfusate and lung is monitored and maintained at normothermic temperature.

b. At the completion of an EVLP procedure, the perfusate is rapidly cooled to ~10°C prior to repackaging for cold storage and transportation to a medical facility for transplant.

3. From the heat exchanger, the perfusate goes through the membrane, oxygenator, which is connected to a deoxygenation gas mix (86% N_2, 8% CO_2, 6% O_2) where the dissolved O_2 in the circuit diffuses out of the perfusate to produce a lower physiologic level representative of venous blood prior to re-entering the lungs.

a. A (non-fluid contacting) temperature probe is attached to the oxygenator outlet line to monitor the temperature of perfusate entering the lung. The temperature is measured and displayed by the perfusion system.

4. From the membrane oxygenator, the perfusate passes through a leukocyte filter just before it enters the lung via the pulmonary artery (PA) lung cannula.

a. The leukocyte filter functions to reduce the number of microaggregates, micro-emboli, and activated leukocytes circulating back through the donor lung.

b. A (non-fluid contacting) flow sensor is attached to the tubing connected to the PA cannula and monitors the flow rate (LPM) of the deoxygenated perfusate going into the lung.

c. A pressure line in the PA lung cannula that is connected to the pressure Monitor via a pressure transducer at the point of interface between the cannula and lung to measure the PA pressure (PAP).

5. The oxygenated perfusate exits the lung through the LA lung cannula.

a. A pressure line in the LA lung cannula is connected to the perfusion system via a pressure transducer to measure and monitor the LA pressure (LAP).

b. A (non-fluid contacting) temperature probe is attached at the reservoir inlet to monitor the temperature of perfusate exiting the lung.

6. Any perfusate leaking from the lung drains into the organ chamber and is directed back into the hardshell reservoir via a roller pump *(not shown in Figure 1 above*).

7. Samples from the LA and PA lines via the sample manifold are taken for testing of pH, PCO_2, PO_2, lactate, and glucose, using the ABG analyzer *(not shown in Figure 1 above*).

8. The cycle repeats during the EVLP procedure until a determination is made by the prescribing physician to either accept or decline the lung for transplant*(not shown in Figure 1 above*).

    a. Every hour throughout the procedure, the EVLP circuit is drained of a prescribed volume of perfusate via the leukocyte filter drain line and replenished with an equal volume of fresh perfusate added to the hardshell reservoir.

Several ancillary components are used to support the assembly and set-up for use, and use of the LungFX to perform the EVLP procedure. Please refer to the LungFX Users Guide for a list of the ancillary components.

Please refer to the LungFX Users guide for a complete description of each device component and properties relevant for the Intended Use.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Standard of care processes for evaluation of donor lung function typically take place within the donor patient's body prior to surgical procurement of the organ. These evaluation techniques and methods are similar to those used ex vivo with the LungFX device. If a decision is made to transplant the organ, then the organ will be placed in cold static storage consisting of a cold solution indicated for lung preservation and transported in a container to the recipient's transplant center. During the standard of care process the organ experiences one cold ischemic time (amount of time the organ is kept cold without oxygen or nutrients) after organ harvesting but prior to transplantation into the recipient. The longer the cold ischemic time the greater the ischemic injury which can lead to tissue damage and worse transplant outcomes.

There are 2 other marketed devices for ex vivo perfusion of donor lungs, the TransMedics® Organ Care System™ (OCS) Lung System (P160013) and the XVIVO Perfusion System™ (XPS) with STEEN Solution Perfusate (P180014). The OCS is a portable, normothermic organ perfusion, ventilation, and monitoring medical device indicated for preservation of standard criteria donor lung pairs and for preservation of donor lung pairs initially deemed unacceptable for procurement and transplantation based on limitations of cold static preservation. The XPS is indicated for use in flushing and temporary continuous normothermic machine perfusion of initially unacceptable excised donor lungs during which time the ex vivo function of the lungs can be reassessed for transplantation. Each of these devices allow for ex vivo assessment of donor lungs prior to transplantation.

VII. MARKETING HISTORY

The LungFX has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

LungFX is indicated for use with explanted donor lungs that cannot be placed for transplant by an Organ Procurement Organization with any of the matched candidates when using direct-to-recipient procurement and preservation procedures. While there is no direct patient contact with this device when it is used as labeled, the device has direct contact with the lungs that are subsequently transplanted into the recipients. Therefore, donor lung quality after assessment and preservation may have a potential effect on allograft function and survival.

The potential for contamination and mechanical trauma due to the manipulation and cannulation of the lung airway and vascular structures may lead to complications after transplantation.

Patients receiving a lung evaluated with LungFX may experience adverse events (AEs) including those experienced with any lung transplant.

Below is a list of some of the AEs observed during clinical studies of the device.

- Death
- Primary graft dysfunction (PGD)
- Chronic lung allograft dysfunction (CLAD)
- Respiratory failure
- Lung transplant rejection
- Pulmonary embolism
- Pneumonia
- Bronchostenosis
- Hypoxia
- Dysphagia

These AEs were also observed in transplant recipients whose lungs did not undergo evaluation with the LungFX device prior to transplantation. For the specific AEs that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

Non-clinical studies performed included electromagnetic compatibility testing, design verification and validation activities, and human factors/usability validation, which collectively evaluated the system’s conformity to design requirements, intended use, and user needs. Testing was conducted using production-equivalent configurations under representative and worst-case conditions, in accordance with applicable regulatory standards and recognized consensus guidelines. The results demonstrate that LungFX meets predefined acceptance criteria for essential performance, safety, and usability, and supports its use in the intended operating environments. Summaries of these studies are detailed below.

In addition to non-clinical studies performed by the Sponsor, the LungFX device utilizes off-the-shelf components that are the subject of existing 510(k) clearances. Those pre-market notifications include information regarding biocompatibility, shelf-life, and instructions for reprocessing. LungFX labeling incorporates relevant instructions for use, storage and shelf-life, and cleaning/reprocessing instructions provided by the manufacturers of the LungFX components.

A. Laboratory Studies

Electromagnetic Compatibility (EMC) Testing

The Sponsor conducted a gap assessment evaluating compliance with IEC 60601-1 General requirements for basic safety and essential performance, specifically comparing Amendment 1 (2012) of the standard with Amendment 2 (2021). The gap assessment confirmed that, with respect to Part 1 of the standard, each device component is certified to its applicable particular and collateral standard.

With respect to Part 2 of the standard, the Sponsor performed electromagnetic compatibility (EMC) testing on LungFX in accordance with IEC 60601-1-2 and related IEC 61000 standards to evaluate basic safety and essential performance under electromagnetic disturbances. The objective of testing was to confirm that the system maintains essential performance, including perfusion, ventilation, temperature control, monitoring, and alarm functionality, in the intended operating environment. Testing was conducted on four representative production-equivalent component systems: the perfusion system, heater-cooler unit, ventilator, and ABG analyzer.

Testing included electrostatic discharge, radiated and conducted immunity, electrical fast transient/burst, surge, magnetic field immunity, voltage dips, and emissions. Predefined acceptance criteria required maintenance of essential performance (e.g., flow accuracy, temperature stability, ventilation delivery, and alarm capability). All tests met applicable criteria and were reported as passing. Minor transient anomalies were observed during early testing but were either self-resolving or mitigated through corrective actions and successful retesting. Overall, LungFX demonstrated compliance with EMC requirements and maintained safe and effective performance under expected electromagnetic conditions.

Human Factors / Usability Engineering Validation

Human factors validation testing was conducted to evaluate safe and effective use of LungFX under representative conditions. A simulated-use study was performed with 15 trained users working in teams of 3, representing intended operators. The objective was to assess performance of critical tasks including setup, operation, monitoring, and completion of EVLP procedures. Predefined success criteria evaluated correct task execution and absence of critical use errors.

All participants successfully completed simulated procedures and all critical tasks. Minor use events were observed but were either self-corrected or did not impact safety or effectiveness. Root cause analyses indicated normal user variability, and residual risks were determined to be acceptable. No deviations impacted study validity. Results demonstrate that the device supports safe and effective use by intended users.

Design Verification and Validation

Design verification and validation (DV&V) activities for LungFX were conducted to confirm that the final device configuration meets established design requirements, user needs, and intended use under representative conditions. Verification activities evaluated conformity of design outputs to design inputs through bench testing, analysis, inspection, and subsystem qualification, while validation activities assessed system performance and usability under simulated use conditions. All testing was performed using production-equivalent configurations and in accordance with applicable regulatory requirements, recognized consensus standards, and internal quality procedures. The following sections summarize the key domains of DV&V testing, including verification, EMC and electrical safety, system validation, human factors integration, and risk management, along with their respective results and conclusions.

1. *Verification Testing*

   Design verification activities were performed to confirm that the LungFX configuration meets defined design requirements. Methods included bench testing, inspection, and subsystem qualification using production-equivalent units for the perfusion system, heater-cooler unit, ventilator, and ABG analyzer. Acceptance criteria were predefined based on system performance specifications such as flow, pressure, temperature, and analytical accuracy. All verification activities met acceptance criteria with no outstanding nonconformances.

2. *EMC and Electrical Safety Verification*

   Verification included EMC and electrical safety testing in accordance with IEC 60601-1-2 and recognized safety standards. The system demonstrated immunity to electromagnetic disturbances including ESD, surge, and RF exposure. All acceptance criteria were met, and transient anomalies observed during initial testing were resolved without impact to final system performance.

3. *System Validation*

   Design validation was conducted using simulated-use EVLP procedures to demonstrate that the device meets user needs and intended use. Testing included multiple EVLP runs with representative donor lungs. Results confirmed stable

perfusion, controlled temperature (37°C ± 1°C), proper ventilation, and integration of monitoring and alarms. All predefined performance criteria were achieved.

4. *Human Factors Integration*

Human factors validation confirmed that trained users can complete all critical tasks safely and effectively. Simulated-use testing demonstrated successful completion of setup, operation, monitoring, and shutdown tasks. Observed use events were minor and did not result in unacceptable risk, confirming adequacy of usability controls.

5. *Risk and Traceability*

Risk management activities confirmed that all identified risks were mitigated to acceptable levels. Complete traceability from user needs through design inputs, verification, validation, and risk controls was established. Overall, DV&V activities demonstrate that LungFX meets design and performance requirements and is suitable for intended use.

Below is a table summarizing the non-clinical testing performed by the Sponsor discussed in more detail above.

Table 2: Summary of Non-Clinical Testing

Test	Purpose	Acceptance Criteria	Results
Electromagnetic Compatibility	To evaluate basic safety and essential performance under electromagnetic disturbances	Maintain essential performance using IEC 60601-1-2 test methods (4 samples)	All tests passed
Human Factors / Usability Engineering Validation	To evaluate representative users' ability to safely and effectively use LungFX under representative conditions	Successful task completion in a simulated-use study (15 users)	All critical tasks completed
Device Verification and Validation	To confirm that the final device configuration meets established design requirements, user needs, and intended use under representative conditions	Bench, validation, and subsystem testing meet design requirements and user needs (minimum of 3 data points collected for each test)	All tests passed

X. SUMMARY OF CLINICAL STUDIES

Three clinical studies were used to establish a reasonable assurance of safety and effectiveness of EVLP with the LungFX device for centralized, *ex vivo* (outside the body) evaluation of deceased-donor lungs (single and double) that cannot be placed for transplantation by an Organ Procurement Organization (OPO) with any of the matched candidates if using direct-to-recipient procurement and preservation procedures. LungFX provides normothermic perfusion and ventilation of procured donor lungs initially stored with cold static preservation solution.

LungFX is intended to allow for re-assessment, in a controlled environment, of procured donor lungs' suitability for transplantation into male and female patients aged 18 years or older with end-stage lung disease awaiting first time (double or single) lung transplantation. Lungs accepted for transplantation after LungFX require a second period of storage with cold static preservation solution, and cumulative preservation time of transplanted lungs is not intended to exceed 20 hours. The first study was conducted in Canada and the other two were conducted in the United States (US) under IDEs, G140021 and G170312. G140021 was a feasibility study and data obtained from this trial was used to inform study design and support approval for the pivotal study conducted under G170312. Data from the pivotal clinical study were the basis for the PMA approval decision.

A summary of the clinical studies is presented below.

Canadian HELP Study (Single-Center)

The Canadian HELP study (NCT01190059) was a prospective, non-randomized, single-center study that reviewed clinical outcomes in study subjects receiving initially declined donor lungs treated with 4 hours of EVLP using STEEN Solution delivered using off-the-shelf cardiopulmonary bypass equipment. The equipment and STEEN Solution became known as the Toronto EVLP System (TES) and this device was licensed for use in LBE's clinical studies, being renamed the Centralized Lung Evaluation System (CLES) (Brand Name: LungFX) for the subsequent pivotal study. The primary endpoint of the HELP study was the incidence of ISHLT-defined primary graft dysfunction (PGD) Grades 2 and 3 at 72 hours after transplantation. The results were compared to those in a control arm consisting of all available standard-of-care transplant recipients at the same institution transplanted during the study period (2008-2010). PGD Grade 2 at 72 hours was 11% and 23%, and PGD Grade 3 at 72 hours was 3% and 11% for the EVLP and Control Groups, respectively. Following a compassionate use extension of the study, Health Canada approved STEEN Solution for use with off-the-shelf medical equipment to perform EVLP in 2012. One year survival in the EVLP arm (n=49) of the study was 83.7% compared to 85.1% in the control arm (n=262).

Traditional Feasibility Study- PXUS 14-001

After the Canadian HELP study, FDA approved a US feasibility study (PXUS 14-001, IDE G140021), referred to as the Traditional Feasibility Study, which was intended to establish preliminary safety and collect exploratory data. The device and EVLP procedure used in this study were identical to the TES device used for the HELP study. This study also provided a longer-term cohort of recipients followed for 5 years after transplant under a Data Use Agreement with United Network for Organ Sharing (UNOS) that provided access to the federal Organ Procurement and Transplantation Network (OPTN) database.

A. Study Design

PXUS 14-001 was an unblinded, non-randomized, feasibility study. EVLP with TES (later redesignated as the "CLES" which was changed to "LungFX") was performed exclusively by the Sponsor at the Sponsor's facility with the same EVLP device used in the subsequent pivotal study. The study included male and female lung transplant recipients, requiring first-time SLT or DLT, who were at least 18 years of age, and were not receiving mechanical ventilation, ECMO, or other extracorporeal life support (ECLS) at the time of initial lung offer.

Patients received a transplant with either lungs preserved and assessed on the EVLP device (EVLP group) or a conventional lung transplant (non-EVLP group) preserved using static cold storage only. Patients who received a non-EVLP lung transplant were matched to the EVLP group with respect to transplant center, Single or Double Lung transplant (SLT or DLT, respectively), and Lung Allocation Score Disease Diagnosis Group. The primary safety endpoints were PGD 3 at 72 hours after transplant and 30-day mortality.

Patients were treated between July 2015 and October 2018. The database for this study reflected data collected through January 13, 2020 and included 118 patients (66 EVLP and 52 non-EVLP). There were 8 investigational sites with 7 that transplanted at least 1 lung following evaluation with the TES. The EVLP group consisted of 31 SLT subjects and 35 DLT subjects and the non-EVLP group consisted of 21 SLT subjects and 31 DLT subjects. The study database was locked for analyses of endpoints after the last subject completed their last visit at 12 months, on November 07, 2019, and all ongoing AEs were followed until resolution or for 30 days after the subject's last Study Center visit, whichever occurred first.

B. Feasibility Study Results

The incidence of PGD 3 at 72 hours was substantially higher in the EVLP group (24.2%) compared to the non-EVLP group (3.8%), primarily as a consequence of more post-transplant ECMO use in the EVLP group.

All subjects that received a lung transplant in this study survived to Day 30. At 1 year post-transplant, survival was 89.4% in the EVLP group and 92.3% in the non-EVLP group.

Subjects in the study were followed for 5 years post-transplant via the OPTN database, and survival status for all subjects was complete. Survival for years 2 through 5 post-transplant are presented in Table 3. At 5 years, the survival rates in both arms were similar.:

Table 3: Feasibility study (PXUS-14-001) Patient Survival Results

Follow up	Subject Status	EVLP			Control		
		SLT (N=31)	DLT (N=35)	Overall (N=66)	SLT (N=21)	DLT (N=31)	Overall (N=52)
<= 1 Year Post-Transplant	Living	29 (93.5%)	30 (85.7%)	59 (89.4%)	20 (95.2%)	28 (90.3%)	48 (92.3%)
	Dead	2 (6.5%)	5 (14.3%)	7 (10.6%)	1 (4.8%)	3 (9.7%)	4 (7.7%)
	Not Reported	0	0	0	0	0	0
2 Year Post-Transplant	Living	28 (90.3%)	29 (82.9%)	57 (86.4%)	15 (71.4%)	25 (80.6%)	40 (76.9%)
	Dead	3 (9.7%)	6 (17.1%)	9 (13.6%)	6 (28.6%)	6 (19.4%)	12 (23.1%)
	Not Reported	0	0	0	0	0	0
3 Year Post-Transplant	Living	24 (77.4%)	26 (74.3%)	50 (75.8%)	14 (66.7%)	25 (80.6%)	39 (75.0%)
	Dead	7 (22.6%)	9 (25.7%)	16 (24.2%)	7 (33.3%)	6 (19.4%)	13 (25.0%)
	Not Reported	0	0	0	0	0	0
4 Year Post-Transplant	Living	16 (51.6%)	24 (68.6%)	40 (60.6%)	10 (47.6%)	22 (71.0%)	32 (61.5%)
	Dead	15 (48.4%)	11 (31.4%)	26 (39.4%)	11 (52.4%)	9 (29.0%)	20 (38.5%)
	Not Reported	0	0	0	0	0	0
5 Year Post-Transplant	Living	12 (38.7%)	21 (60.0%)	33 (50.0%)	9 (42.9%)	19 (61.3%)	28 (53.8%)
	Dead	19 (61.3%)	14 (40.0%)	33 (50.0%)	12 (57.1%)	12 (38.7%)	24 (46.2%)
	Not Reported	0	0	0	0	0	0

CLES Pivotal Study

A pivotal clinical study, EVP-DEV-LTX-301 (referred to as the CLES Pivotal Study) was conducted to establish reasonable assurance of safety and effectiveness of the CLES (Brand Name: LungFX) device under IDE G170312. Data from the CLES Pivotal Study are the principal basis for the PMA approval decision. A summary of the CLES Pivotal Study is presented below. Clinical results from the HELP and Traditional Feasibility Studies were used to inform the pivotal study's study design and statistical analysis plan. The primary objective of the CLES Pivotal Study was to establish the safety and effectiveness of LungFX to evaluate lungs that would not otherwise be used for transplantation.

A. Study Design

The CLES Pivotal Study, was a prospective, multicenter, open-label, non-randomized study that tracked post-transplant patient management, survival, and reported AEs among

recipients of lungs that underwent EVLP with the LungFX device (the EVLP group) and among contemporaneous recipients of lungs that did not undergo EVLP with the LungFX device (non-EVLP group); the contemporaneous non-EVLP recipients were prospectively matched based on pre-specified characteristics (see below), and EVLP recipients were also compared to aggregate contemporaneous results from the Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients (OPTN/SRTR) The Primary Endpoint was twelve-month survival within the EVLP group, with a comparison of the EVLP group's twelve-month survival against a pre-specified performance goal; the US Food and Drug Administration (FDA) had indicated that powered hypothesis-testing of the primary endpoint would be necessary to appropriately inform a benefit-risk assessment of the device. The target sample size for the study was 93 subjects in the EVLP group. Safety and effectiveness measures were further assessed by comparing matched cohorts from the EVLP and non-EVLP groups; 75 EVLP subjects were to be matched 1:1 on the following characteristics to the non-EVLP subjects:

- Transplant Center
- Transplant Type (SLT or DLT)
- Lung Allocation Score Disease Diagnosis Group (A, B, C, or D)
- Pre-operative use of ECMO

Unlike the feasibility study, the pivotal study's protocol explicitly allowed for inclusion of donor lungs conventionally classified as "extended criteria" or "standard criteria" (see below), but this parameter was not a component of the matching process. There was a total of 18 investigational sites, 12 of which transplanted at least 1 lung following evaluation with the LungFX device. Patients were transplanted between April 2019 and December 2022. The database for the CLES Pivotal Study reflects data collected through 29 March 2024 and included 174 patients (94 EVLP, 80 non-EVLP). The study database was locked for analyses of endpoints after the last subject completed their last visit at 12 months, and all ongoing AEs were followed until resolution or for 30 days after the subject's last Study Center visit, whichever occurred first. FDA had indicated that longer-term recipient survival data would be informative and recommended their collection; these data were obtained from an OPTN/SRTR database query as of 31 March 2025.

A Data Monitoring Committee (DMC), independent of the Sponsor, was established to monitor subject safety, as well as advise the Sponsor on potential decisions for stopping the study prematurely concerning either EVLP futility or effectiveness as observed in this study. Over the course of the study, when reviewing the safety data, the DMC identified no safety concerns that warranted Sponsor action.

A separate Clinical Events Committee (CEC), independent of both the Sponsor and DMC, was charged with adjudicating the relatedness of investigator-reported serious adverse events (SAEs) to EVLP, lung transplantation, and ECMO usage, as well as all deaths reported for a determination of lung graft-related mortality. Adjudication was blinded to transplant group to the extent possible for an open-label study.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the CLES Pivotal Study was limited to the donor lungs and transplant recipients that met the following criteria.

Donor Lung Inclusion and Exclusion Criteria (Pre-EVLP)

Eligible donor lungs included both "standard criteria" and "extended criteria" donor organs. Extended criteria donor lungs were defined as either donation after circulatory death (DCD) or as having two or more of the following:

- Final PaO_2/FiO_2 <300 mmHg
- Age at death >55 years
- Greater than or equal to 20 pack-year smoking history
- Diabetes mellitus diagnosis
- Evidence of blood infection
- Abnormal chest x-ray or computed tomography
- Evidence of pulmonary edema

Donor lungs that did not meet extended criteria were considered "standard" for the purposes of subgroup analysis.

The donor lung and referral process is described in Figure 2 below. Donor lungs were eligible for EVLP evaluation if an Organ Procurement Organization (OPO) verified that those lungs would not otherwise be used for transplantation. Donor lungs could be referred to LBE for EVLP by either a study center investigator or the participating OPO. The protocol did not limit the reasons why donor lungs were determined to be otherwise unusable. However, in all cases OPOs were asked to provide the reason(s) why the lungs would not otherwise be used; common reasons included one or more of the following:

- Allocation ended: attempts to place the lungs via match run sequence yielded refusal responses to standard (non-EVLP) offers and the OPO concluded that the lack of remaining allocation time supported the decision for EVLP
- Logistics: the OPO did not have time to perform/complete a lung-specific match run. For example, the overall organ donation process may have been accelerated due to donor deterioration, limited operating room availability, donor family request, procurement teams with recipient urgency for other organs, other competing issues requiring donor surgery to be scheduled prior to lung placement, or another procurement team recovering the lungs for an accepting center
- DCD
- Operating room decline: an unexpected suitability issue was identified at the time of procurement resulting in a decision that the previously designated recipient was no longer appropriate, which also severely limited time for the OPO to reallocate the lungs

- Recipient availability: after procurement started, the original intended recipient was unable to receive the transplant, creating a critical timing challenge for the OPO to reallocate the lungs
- Other: the OPO determined the lungs would not otherwise be used for transplant for reasons not listed above; in these cases, additional details were provided to verify the lungs met study criteria before proceeding to EVLP

Donor lungs were ineligible for EVLP evaluation if 1 or more of the following criteria were met:

- Confirmed pneumonia and/or persistent purulent secretions identified via bronchoscopy prior to donor lung excision
- Confirmed evidence of aspiration
- Significant mechanical lung injury or trauma
- HIV or active Hepatitis C
- The initial cold ischemic time (CIT-1, the time period spanning donor aortic cross-clamp/initial flush to start of EVLP), which includes organ shipment from the donor site to the Sponsor, estimated to be >10 hours

Donor Lung Inclusion Criteria (Post-EVLP)

To be eligible for transplantation, the donor lung(s) had to complete EVLP, be accepted by the Investigator, and meet the following 3 criteria:

- At least 1 of the following 2 standard clinical criteria for transplantation were met at final assessment on the LungFX device:

  a. Partial pressure of oxygen in arterial blood (PaO_2)/FiO_2 ≥300 mmHg at the end of EVLP; or

  b. PAP, pulmonary vascular resistance (PVR), and peak airway pressure measurements defined as stable or no more than 20% worse than the Hour 1 assessment (baseline) compared to measurements at the end of EVLP;

- The transplant physician was clinically satisfied with the lung evaluation; and

- Purulent secretions identified via bronchoscopy prior to donor lung excision, but not considered persistent (i.e., were clear by the Hour 3 assessment).

Donor lungs were evaluated for transplant suitability by the Investigator, in consultation with the EVLP team, but ultimately it was the responsibility of the Investigator to accept or decline lungs for the intended recipient.

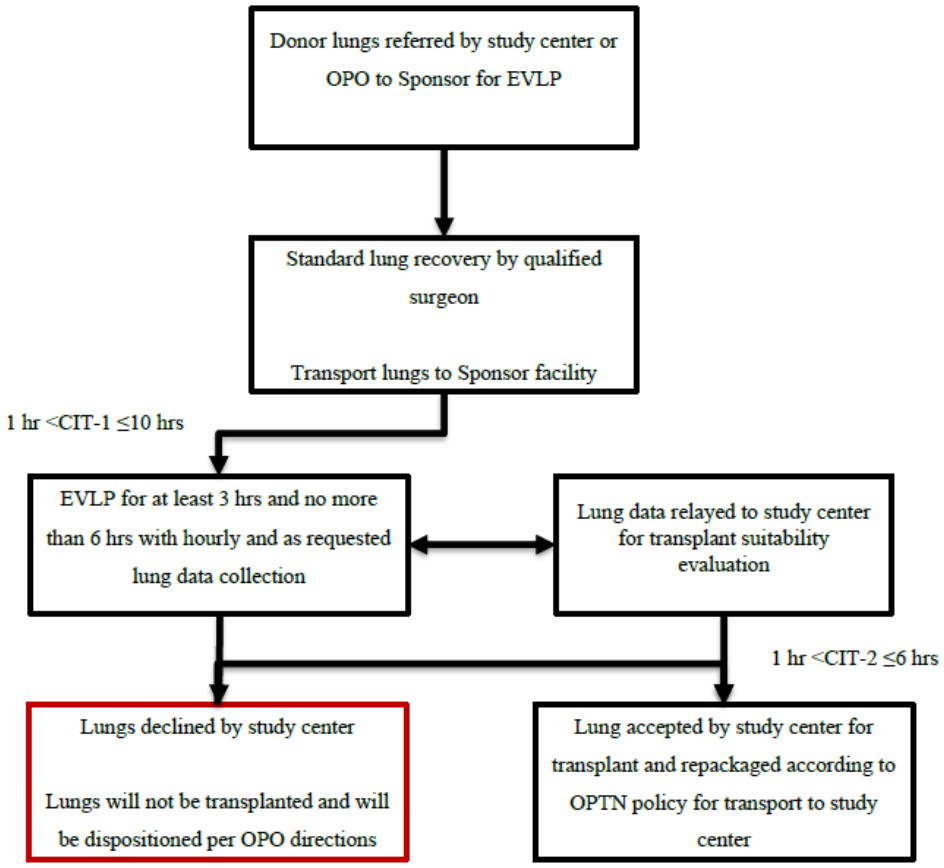


Figure 2: Donor Lung Referral and Evaluation Process

For SLT and the first lung of DLT, the maximum allowed total preservation time was 22 hours.

The maximum allowed preservation time for the second lung of DLT was 26 hours.

Clinical Subject (Recipient) Inclusion and Exclusion Criteria

Enrollment in the study was limited to patients who met the following inclusion criteria:

- 18 years of age or older
- Male or female
- Actively awaiting a SLT or DLT
- Provided informed consent for participation in the study prior to participating in any study-related assessments or procedures
- Matched with and underwent transplantation of a donor lung

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Listed for same-side lung re-transplantation
- Listed for multiple organ transplantation (lung + any other organ)
- Listed for live donor lobar lung transplant
- Positive for HIV or *Burkholderia cenocepacia* infection
- Received a standard-of-care (non-EVLP) lung transplant, but did not match to an EVLP subject per matching characteristics above
- Transplanted with a lung that used another EVLP technology
- Current participation in another respiratory or cardiovascular clinical study

2. Screening and Follow-up Schedule

Potential study subjects were screened at any time up to 1 year prior to the day of the lung transplant procedure. The Post-Intervention Period was defined as 12 months or until the initial hospital discharge post-transplant, whichever occurred last. During this period, there were 7 formal study visits that occurred at 24, 48, and 72 hours, as well as Day 30, Day 90, and at Months 6 and 12, post-transplant. During each visit, subject-specific data were collected to inform aggregate safety and effectiveness analyses. Data for longer-term survival was obtained from the OPTN/SRTR registry.

3. Clinical Endpoints

I. Primary Endpoint

The primary endpoint was the 12-month survival rate post-transplant.

The Primary Endpoint's statistical analysis was calculation of the posterior probability of EVLP 12-month survival being greater than a pre-specified performance goal, which LBE set at 81.2%. The Primary Endpoint's statistical hypothesis would be met if the posterior probability was greater than 0.95.

II. Secondary Endpoints

The secondary endpoints for both the EVLP and non-EVLP groups included:

- Adjudicated lung graft-related mortality, measured as the percentage of subject deaths determined to be directly or indirectly related to the transplanted organ
- 2016 International Society for Heart and Lung Transplantation (ISHLT) primary graft dysfunction (PGD) score (Grades 0 to 3) at Hours 0 (ICU admission), 24, 48, and 72 post-transplant
- Subject survival at Days 30 and 90 and at Months 6 and 12 post-transplant
- Rate of CLAD within one year post-transplant, measured as the percentage of subjects diagnosed with CLAD at Day 90, 6 months and 12 months
- Duration of ventilator support, measured as the total number of hours where subject required ventilator support prior to the initial hospital discharge post-transplant

- Rate of ECMO use, measured as the proportion of subjects that required ECMO support for any reason, at any time prior to the initial hospital discharge post-transplant
- ICU length of stay (LOS), measured as total number of days in the ICU until the initial hospital discharge post-transplant, inclusive of ICU readmissions during initial hospitalization
- Hospital LOS, measured as the total number of days in the hospital until initial discharge post-transplant
- Extended evaluation and preservation time, defined as the elapsed time between donor aortic cross-clamp at procurement and placement of the first stitch in the anastomosis at transplant (recorded separately for each lung in a DLT)
- Rate of respiratory failure
- Forced expiratory volume in 1 second (FEV_1)

The following secondary endpoints were evaluated for the EVLP group only:

- Assessment of reported AEs of LungFX lung transplants during subject participation in the study
- Utilization rate of EVLP lungs, measured as the number of EVLP procedures resulting in lungs accepted for transplant divided by the number of EVLP procedures performed on lungs referred for EVLP
- Increase in use of donor lungs, measured by the number of lungs referred for EVLP and accepted for transplantation at a study center without the use of EVLP

Although not a Secondary endpoint, Adverse Events were captured and compared between the EVLP and non-EVLP groups.

Subgroup Analyses

Supplemental analyses of all primary and secondary endpoints were pre-specified for the following subgroups:

- Donor lung criteria (extended or standard)

  Extended criteria donor lungs were defined as meeting the following:

  - Donation after circulatory death (DCD); or
  - Two or more of the following:
    - Final PaO2/FiO_2 <300 mmHg
    - Age at death >55 years
    - Greater than or equal to 20 pack-year smoking history
    - Diabetes mellitus diagnosis
    - Evidence of blood infection

- Abnormal chest x-ray or computed tomography
- Evidence of pulmonary edema

Donor lungs that did not meet extended criteria were considered standard criteria.

- SLT or DLT
- CIT-1: first (pre-EVLP) cold ischemia time (first lung and second lung)
- CIT-2: second (post-EVLP) cold ischemia time (first lung and second lung)
- Total preservation time (TPT): CIT-1 + EVLP preservation + CIT-2 (first lung and second lung)
- Recipient pre-operative ECMO (use or non-use)
- Donor lung EVLP referral source (OPO or transplant clinician)
- Study center enrollment numbers (high-enrollment or low-enrollment)

B. Accountability of the CLES Pivotal Study Cohorts

There were 642 wait-listed lung transplant candidates screened for enrollment; with enrollment defined as having provided informed consent (up to one year before transplantation) and having undergone a transplantation procedure. At the time of database lock, 174 (27%) were enrolled into the study and 153 (87.9%) patients were available for analysis at the completion of the study, the 12 month post-operative visit on December 22, 2023. There were no subjects lost to follow-up. All subjects who did not complete the study through the 12-month Post-Intervention Period did not complete the study due to death.

1. Full Analysis Set

The Full Analysis Set (FAS) included all subjects in the EVLP group regardless of subject outcome or subsequent re-transplant. This population was used for the primary analysis and secondary endpoints and safety analyses. There were 94 subjects enrolled in the CLES Pivotal Study who received lungs after EVLP. Data on vital status of all 94 (100.0%) subjects were available for analysis at the completion of the study, Month 12 (Visit 7). No subjects were re-transplanted or lost to follow-up. Note: the FAS is the subset of EVLP subjects within the Ancillary Population Set (below).

2. Ancillary Population Set

The Ancillary Population Set (APS) included all subjects who received either a transplant by EVLP or standard-of-care (i.e., the “non-EVLP group”). This population was used for the safety analyses and as supportive for the primary and secondary endpoints. There were 174 subjects enrolled in the CLES Pivotal Study (94 EVLP, 80 non-EVLP). Data on vital status of all 174 (100.0%) APS subjects were available for analysis at the completion of the study, Month 12 (Visit 7). There were no subjects lost to follow-up. Note: the FAS (above) is the subset of EVLP subjects within the APS.

3. Matched Analysis Set

The Matched Analysis Set (MAS) included all subjects in the APS who received either a transplant by EVLP or standard-of-care and were matched 1:1 across study groups by the criteria previously described. This population was added *post hoc* due to intended 1:1 matching for APS being incomplete at the time of enrollment closure. This population was used as supportive for the primary and secondary endpoints and safety analyses. There were 158 matched subjects enrolled in the CLES Pivotal Study (79 EVLP and 79 non-EVLP). Data on vital status of all 158 (100.0%) MAS subjects were available for analysis at the completion of the study, Month 12 (Visit 7).

4. Study Center Enrollment Numbers

A total of 12 sites enrolled subjects as shown in Table 4 (APS) and Table 5 (MAS) below. The 3 highest enrolling sites collectively enrolled over half of the study's subjects (56% of APS subjects and 57% of MAS subjects).

Table 4: Ancillary Population Set Enrollment

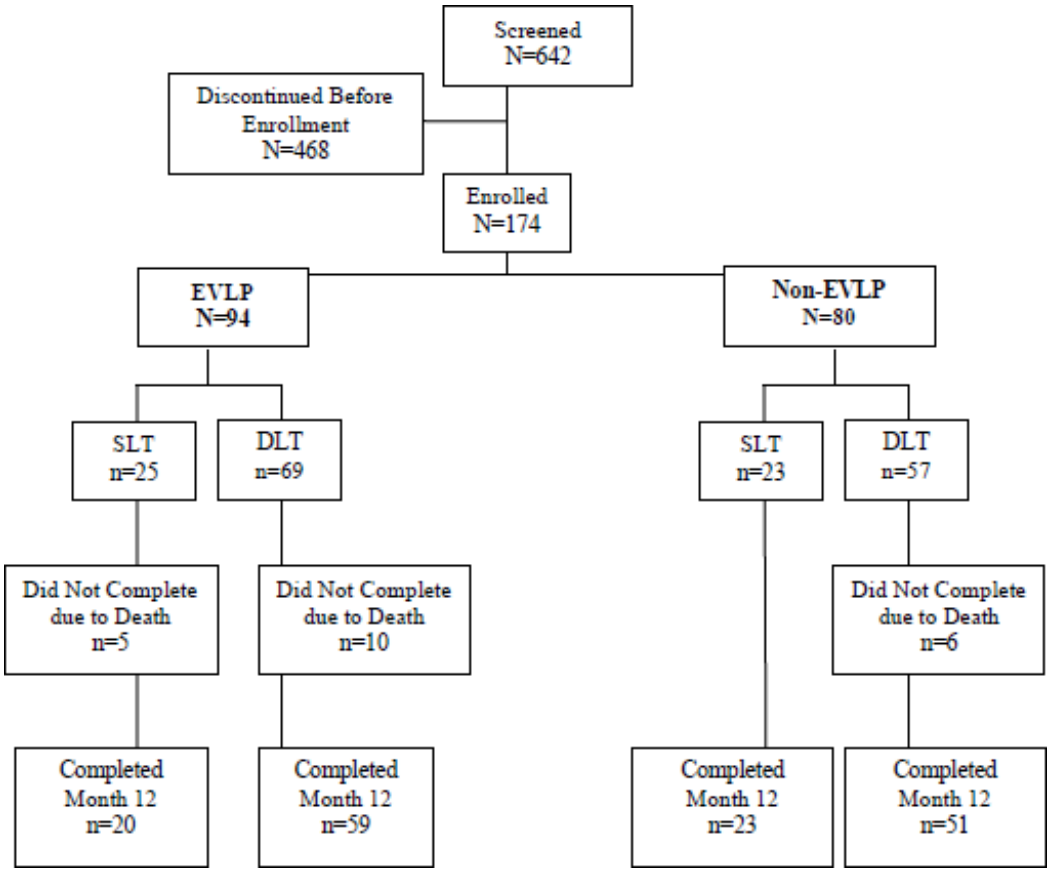
Site Number	Institution Name	EVLP Count	Non-EVLP Count
102	Cleveland Clinic	6	3
103	Mayo Clinic Jacksonville	15	14
105	New York University	6	6
106	Vanderbilt University	18	16
108	Duke University	1	1
109	University of Maryland	11	11
110	INOVA Fairfax	20	15
111	Johns Hopkins University	7	7
112	Newark Beth Israel	2	1
114	University of Michigan	1	1
116	Emory University	2	1
117	Spectrum Health	5	4

Table 5: Matched Analysis Set Population Enrollment

Site Number	Institution Name	EVLP Count	Non-EVLP Count
102	Cleveland Clinic	3	3
103	Mayo Clinic Jacksonville	14	14
105	New York University	5	5
106	Vanderbilt University	16	16
108	Duke University	1	1
109	University of Maryland	11	11
110	INOVA Fairfax	15	15
111	Johns Hopkins University	7	7
112	Newark Beth Israel	1	1
114	University of Michigan	1	1
116	Emory University	1	1
117	Spectrum Health	4	4

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant Source: CLES

A full consort diagram of the study is provided in Figure 3, and Table 6 (APS) and Table 7 (MAS) below.



Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant Source: CLES

Figure 3: Summary of Subject Cohort Disposition - Ancillary Population Set

Table 6: Summary of Subject Cohort Disposition - Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT N=25	DLT N=69	Overall N=94	SLT N=23	DLT N=57	Overall N=80
Completed Study Month 12, n (%)						
Yes	20 (80.0)	59 (85.5)	79 (84.0)	23 (100)	51 (89.5)	74 (92.5)
No	5 (20.0)	10 (14.5)	15 (16.0)	0 (0.0)	6 (10.5)	6 (7.5)
Did Not Complete Study Month 12, n (%)						
Death	5 (20.0)	10 (14.5)	15 (16.0)	0 (0.0)	6 (10.5)	6 (7.5)

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant
Note: Ancillary Population Set included subjects who received either EVLP or standard (non-EVLP) transplant.
Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per group.

Table 7: Summary of Subject Cohort Disposition – Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Completed Study Month 12, n (%)						
Yes	19 (86.4)	49 (86.0)	68 (86.1)	22 (100)	51 (89.5)	73 (92.4)
No	3 (13.6)	8 (14.0)	11 (13.9)	0 (0.0)	6 (10.5)	6 (7.6)
Did Not Complete Study Month 12, n (%)						
Death	3 (13.6)	8 (14.0)	11 (13.9)	0 (0.0)	6 (10.5)	6 (7.6)

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant
Note: Matched Analysis Set included subjects who received either EVLP or standard (non-EVLP) transplant.
Note: Percentages were based on the total number (N) of subjects in the Matched Analysis Set per group.

C. Study Population Demographics and Baseline Parameters

Recipients

Eighty five of the 94 (90%) EVLP recipients had been on the waiting list for less than one year, while 74 of the 80 (93%) non-EVLP recipients had been on the waiting list for less than 1 year. Medians, means, and ranges of Lung Allocation Scores (LAS) were very similar for EVLP and non-EVLP groups, both at the time of initial listing and at the time of lung matching.

The demographics of the study population are shown in Table 8 (APS) and (MAS) below. Of the 174 lung transplant recipients in this study, the median age at enrollment was 60 years (range: 23 to 75) in the EVLP group and 64 years (range: 24 to 74) in the non-EVLP group. Subjects undergoing SLT tended to be older than subjects who underwent DLT.

In the APS, the majority of subjects enrolled were male, 62/94 (66.0%) subjects in the EVLP group and 48/80 (60.0%) in the non-EVLP group. There were 9/94 (9.6%) subjects in the EVLP group using ECMO at the time of initial lung allocation, whereas 3/80 (3.8%) in the non-EVLP group were on ECMO. In both groups, most recipients were Lung Allocation Score Disease Diagnosis Group (LASDDG) D (Restrictive Lung Disease), consistent with the representation of LASDDGs on the OPTN waiting list.

Table 8: Summary of Subject (Recipient) Demographics and Baseline Characteristics – Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
Age at Transplantation (Years)						
Mean	64.6	55.7	58.0	67.3	59.3	61.6
SD	6.45	10.48	10.33	3.75	10.70	9.92
Median	65.0	58.0	60.0	67.0	61.0	64.0
Min – Max	55 - 75	23 - 73	23 - 75	59 - 72	24 - 74	24 - 74
Sex, n (%)						

Male	21 (84.0)	41 (59.4)	62 (66.0)	14 (60.9)	34 (59.6)	48 (60.0)
Female	4 (16.0)	28 (40.6)	32 (34.0)	9 (39.1)	23 (40.4)	32 (40.0)
Race, n (%)						
Asian	0 (0.0)	2 (2.9)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
Black or African American	2 (8.0)	15 (21.7)	17 (18.1)	1 (4.3)	13 (22.8)	14 (17.5)
White	21 (84.0)	49 (71.0)	70 (74.5)	18 (78.3)	43 (75.4)	61 (76.3)
Unknown	1 (4.0)	3 (4.3)	4 (4.3)	2 (8.7)	0 (0.0)	2 (2.5)
Other	1 (4.0)	0 (0.0)	1 (1.1)	2 (8.7)	1 (1.8)	3 (3.8)
Ethnicity, n (%)						
Hispanic or Latino	2 (8.0)	2 (2.9)	4 (4.3)	4 (17.4)	2 (3.5)	6 (7.5)
Not Hispanic or Latino	23 (92.0)	67 (97.1)	90 (95.7)	19 (82.6)	55 (96.5)	74 (92.5)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Height (cm)[a]						
Mean	173.25	170.08	170.92	167.86	172.12	170.89
SD	9.781	10.849	10.617	10.131	9.226	9.627
Median	173.00	170.20	172.00	170.20	175.00	172.50
Min – Max	148.6 - 194.0	117.8 - 190.5	117.8 - 194.0	147.3 - 182.9	152.4 - 190.5	147.3 - 190.5
Weight (kg)[a]						
Mean	83.49	78.71	79.98	74.51	79.02	77.72
SD	14.446	15.103	15.005	14.262	14.877	14.757
Median	79.00	79.20	79.10	68.30	81.60	80.10
Min - Max	62.6 - 121.4	48.5 - 116.0	48.5 - 121.4	56.1 - 100.1	41.5 - 103.4	41.5 - 103.4
Category	**EVLP**			**Non-EVLP**		
	SLT (N=25)	**DLT (N=69)**	**Overall (N=94)**	**SLT (N=23)**	**DLT (N=57)**	**Overall (N=80)**
BMI (kg/m^2)						
Mean	27.73	27.35	27.45	26.31	26.58	26.50
SD	3.424	6.033	5.447	3.481	4.217	4.000
Median	26.29	26.93	26.91	26.51	27.24	26.86
Min - Max	21.6 - 34.1	16.0 - 62.9	16.0 - 62.9	19.8 - 32.4	16.4 - 37.3	16.4 - 37.3
ECMO Use Status at Time of Initial Lung Allocation, n (%)						
Yes	0 (0.0)	9 (13.0)	9 (9.6)	0 (0.0)	3 (5.3)	3 (3.8)
No	25 (100)	60 (87.0)	85 (90.4)	23 (100)	54 (94.7)	77 (96.3)
Lung Allocation Score Disease Diagnosis Group, n (%)						
Group A: Obstructive Lung Disease	2 (8.0)	16 (23.2)	18 (19.1)	1 (4.3)	14 (24.6)	15 (18.8)
Group B: Pulmonary Vascular Disease	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	0 (0.0)	1 (1.3)
Group C: Cystic Fibrosis/Immunodeficient Disorders	0 (0.0)	5 (7.2)	5 (5.3)	0 (0.0)	3 (5.3)	3 (3.8)
Group D: Restrictive Lung Disease	23 (92.0)	47 (68.1)	70 (74.5)	21 (91.3)	40 (70.2)	61 (76.3)
Lung Allocation Score at Time of Waitlist Addition						
Mean	41.303	46.942	45.442	43.212	43.723	43.576
SD	11.2566	18.1469	16.7260	12.6566	15.6120	14.7457
Median	37.110	38.870	38.135	39.300	36.900	37.995
Min - Max	33.00 - 85.91	30.22 - 90.08	30.22 - 90.08	32.70 - 87.90	32.20 - 89.58	32.20 - 89.58
Lung Allocation Score at Time of Lung Match						
Mean	45.589	54.887	52.414	47.445	52.986	51.393

SD	15.9064	22.8604	21.5516	17.2602	21.9369	20.7474
Median	41.000	43.170	41.400	40.830	41.380	41.105
Min - Max	33.59 - 89.14	32.60 - 90.30	32.60 - 90.30	33.30 - 87.90	32.20 - 91.77	32.20 - 91.77

Abbreviations: BMI, body mass index; DLT, double lung transplant; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Height is reported from Screening and weight is reported from the Baseline/Admission Visit.

Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per transplant group.

Table 9: Summary of Subject (Recipient) Demographics and Baseline Characteristics – Matched Analysis Set

	EVLP			Control		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Age at transplantation (years)						
Mean	64.2	57.2	59.1	67.2	59.3	61.5
SD	6.30	9.63	9.34	3.79	10.70	9.94
Median	65.0	59.0	61.0	67.0	61.0	64.0
Min - Max	55–75	23–73	23–75	59–72	24–74	24–74
n	22	57	79	22	57	79
Gender						
Male	18 (81.8%)	34 (59.6%)	52 (65.8%)	14 (63.6%)	34 (59.6%)	48 (60.8%)
Female	4(18.2%)	23(40.4%)	27 (34.2%)	8 (36.4%)	23 (40.4%)	31 (39.2%)
Race						
American Indian/Alaska Native	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Asian	0 (0.0%)	1 (1.8%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Black or African American	2 (9.1%)	13 (22.8%)	15 (19.0%)	1 (4.5%)	13 (22.8%)	14 (17.7%)
Native Hawaiian/Pacific Islander	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
White	19 (86.4%)	40 (70.2%)	59 (74.7%)	17 (77.3%)	43 (75.4%)	60 (75.9%)
Unknown	1 (4.5%)	3 (5.3%)	4 (5.1%)	2 (9.1%)	0 (0.0%)	2 (2.5%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.1%)	1 (1.8%)	3 (3.8%)
Ethnicity						
Hispanic or Latino	1 (4.5%)	1 (1.8%)	2 (2.5%)	4 (18.2%)	2 (3.5%)	6 (7.6%)
Not Hispanic or Latino	21 (95.5%)	56 (98.2%)	77 (97.5%)	18 (81.8%)	55 (96.5%)	73 (92.4%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Height (cm)[a]						
Mean	173.50	169.35	170.50	168.68	172.12	171.16
SD	10.407	11.270	11.129	9.555	9.226	9.386
Median	174.00	170.00	170.20	171.25	175.00	172.70
Min–Max	148.6–194.0	117.0–190.5	117.0–194.0	147.3–182.9	152.4–190.5	147.3–190.5
n	22	57	79	22	57	79
Weight (kg)[a]						
Mean	84.14	79.03	80.46	74.79	79.02	77.84
SD	14.987	15.185	15.210	14.532	14.877	14.812
Median	79.20	78.10	79.00	69.90	81.60	80.70
Min–Max	62.6–121.4	48.5–116.0	48.5–121.4	56.1–100.1	41.5–103.4	41.5–103.4
n	22	57	79	22	57	79
BMI (kg/m)						
Mean	27.86	27.71	27.75	26.12	26.58	26.45
SD	3.537	6.210	5.573	3.442	4.217	4.000

Median	27.19	27.61	27.61	26.49	27.24	26.64
Min–Max	21.6–34.1	17.3–62.9	17.3–62.9	19.8–32.4	16.4–37.3	16.4–37.3
n	22	57	79	22	57	79
ECMO Use Status at time of initial lung allocation						
Yes	0 (0.0%)	3 (5.3%)	3 (3.8%)	0 (0.0%)	3 (5.3%)	3 (3.8%)
No	22 (100%)	54 (94.7%)	76 (96.2%)	22 (100%)	54 (94.7%)	76 (96.2%)
Lung Allocation Score Disease Diagnosis Group						
Group A: Obstructive Lung Disease	1 (4.5%)	14 (24.6%)	15 (19.0%)	1 (4.5%)	14 (24.6%)	15 (19.0%)
Group B: Pulmonary Vascular Disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Group C: Cystic Fibrosis of Immunodeficient Disorders	0 (0.0%)	3 (5.3%)	3 (3.8%)	0 (0.0%)	3 (5.3%)	3 (3.8%)
Group D: Restrictive Lung Disease	21 (95.5%)	40 (70.2%)	61 (77.2%)	21 (95.5%)	40 (70.2%)	61 (77.2%)
Lung Allocation Score at Time of Waitlist Addition						
Mean	41.646	44.727	43.869	43.453	43.723	43.648
SD	11.9592	16.4218	15.2987	12.9003	15.6120	14.8259
Median	36.845	38.140	38.080	39.860	36.900	38.080
Min–Max	33.00–85.91	30.22–88.58	30.22–88.58	32.70–87.90	32.20–89.58	32.20–89.58
n	22	57	79	22	57	79
Lung Allocation Score at Time of Lung Match						
Mean	46.500	52.608	50.907	47.931	52.986	51.578
SD	16.7693	21.9938	20.7508	17.5044	21.9369	20.8132
Median	41.150	40.460	41.000	41.265	41.380	41.380
Min–Max	33.59–89.14	32.60–90.30	32.60–90.30	33.30–87.90	32.20–91.77	32.20–91.77
n	22	57	79	22	57	79

Abbreviations: BMI, body mass index; DLT, double lung transplant; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Height is reported from Screening and weight is reported from the Baseline/Admission Visit.

Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per transplant group.

Donors

A total of 326 deceased donors were referred to LBE for EVLP during the study. There were 135 of the referred donors (41%) declined for EVLP based on the exclusion criteria listed above, and an additional 40 (12%) were declined for transplantation by any investigator after EVLP. There were 131 donor lung referrals (40%) accepted for EVLP and 91 were ultimately accepted for transplantation. However, 60 additional referrals were transplanted without having undergone CLES EVLP; 53 (88%) of these 60 donor lungs were implanted into non-study patients conventionally after in-situ assessments made by investigators.

Of the 326 lung referrals 91 donor lungs (28%); underwent EVLP followed by post-EVLP transplantation, into 94 recipients (3 of the bilateral lungs donated were split between 6 transplant recipients). Overall, 26/91 EVLP donors (29%) were DCD; only 2 non-EVLP donors were DCD. Importantly, commercial use of normothermic machine perfusion of "non-EVLP" group donor lungs was not included in this study, but the Scientific Registry of Transplant Recipients reports that in 2024 18% of all US lung donations were DCD. DCD was in fact the most frequently cited criterion (Table 10) for EVLP referral among FAS subjects (26/94 (28%), with 3 EVLP donors yielding SLT for 6 recipients), followed by intra-operative decline of provisionally accepted non-EVLP donor lungs. One quarter of the referrals were for non-specific "logistical challenges."

Of the 94 EVLP transplantations, 8 (9%) came from lung referrals made to LBE by the OPO, as opposed to by an investigator.

Table 10: Summary of Reasons for EVLP Referral (Full Analysis Set)

Reason for Referral[a]	**n/N(%)**
Donation after Circulatory Death	26/94 (27.7%)
OR Decline	25/94 (26.6%)
Logistical Challenges	23/94 (24.5%)
Allocation Ended	9/94 (9.6%)
Recipient Availability	4/94 (4.3%)
Other (verbatim reasons provided below)	11/94 (11.7%)
Aggressive placement due to low PaO_2	1/11 (0.9%)
Declining Donor PaO_2 w/ susp pulm edema +/- atl	1/11 (0.9%)
Donor instability prior to the OR	1/11 (0.9%)
Low PaO_2	1/11 (0.9%)
NA-NYUC accepted right lung from OR	1/11 (0.9%)
Requesting LungBio due to Medical quality – low PaO_2	1/11 (0.9%)
Study Center Investigator requires assessment	1/11 (0.9%)
Surgeon believes lungs have marginal oxygenation	1/11 (0.9%)
VAFH to place on EVLP due to decline in PaO_2	1/11 (0.9%)
X-ray, CT and gases showing marginal lung	1/11 (0.9%)
No reason provided	1/11 (0.9%)

[a] Subjects may have more than one reason for referral. List of multiple referral reasons include:
103-0033: Logistical Challenges/Recipient Availability
106-0002: Donation after Circulatory Death/OR Decline
110-0007: Logistical Challenges/Recipient Availability
112-0023: Allocation Ended/Recipient Availability

A total of 168 donors provided lungs in this study to 94 recipients in the EVLP group and 80 recipients in the non-EVLP group. Median donor age at death was 41 years (range: 14 to 61) in the EVLP group and 33 years (range: 15 to 59) in the non-EVLP group (Table 11).

Three EVLP donors provided SLT to 6 recipients, and 1 non-EVLP provided SLT to 2 recipients; donor information for 2 non-EVLP recipients was not available because authorization for research was not documented in the donor records. Extended criteria lungs, as defined above, accounted for approximately half (37/77 (48%)) of the donors for the non-EVLP group's APS population. Conversely, the majority of donors in the EVLP group's FAS and APS (68/91 (75%)) were extended criteria.

Among extended criteria donors, 26 of the 68 EVLP (38%) were classified as such on the basis of DCD, whereas only 2 of the 37 (5%) non-EVLP extended criteria donors were DCD.

Table 11: Summary of Donor Demographics and Baseline Characteristics – Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=69)	Overall (N=91)	SLT (N=22)	DLT (N=55)	Overall (N=77)
Donor Lung Criteria, n (%)						
Standard	1 (4.5)	22 (31.9)	23 (25.3)	11 (50.0)	29 (52.7)	40 (51.9)
Extended	21 (95.5)	47 (68.1)	68 (74.7)	11 (50.0)	26 (47.3)	37 (48.1)
Donation After Circulatory Death, n (%)						
Yes	6 (27.3)	20 (29.0)	26 (28.6)	0 (0.0)	2 (3.6)	2 (2.6)
No	16 (72.7)	49 (71.0)	65 (71.4)	22 (100)	53 (96.4)	75 (97.4)
Age at Death (Years)						
Mean	41.3	37.7	38.6	36.6	34.1	34.8
SD	14.08	12.48	12.89	13.69	11.97	12.45
Median	42.5	39.0	41.0	36.5	33.0	33.0
Min - Max	15 - 61	14 - 58	14 - 61	17 - 59	15 - 59	15 - 59
Sex, n (%)						
Male	17 (77.3)	37 (53.6)	54 (59.3)	14 (63.6)	37 (67.3)	51 (66.2)
Female	5 (22.7)	32 (46.4)	37 (40.7)	8 (36.4)	18 (32.7)	26 (33.8)
Race, n (%)						
Asian	1 (4.5)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.8)	1 (1.3)
Black or African American	5 (22.7)	20 (29.0)	25 (27.5)	3 (13.6)	16 (29.1)	19 (24.7)
White	14 (63.6)	43 (62.3)	57 (62.6)	16 (72.7)	32 (58.2)	48 (62.3)
Unknown	2 (9.1)	6 (8.7)	8 (8.8)	2 (9.1)	6 (10.9)	8 (10.4)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.3)
Height (cm)						
Mean	175.87	170.70	171.95	171.46	172.55	172.24
SD	8.161	9.601	9.494	9.925	9.994	9.921
Median	175.13	170.18	173.00	170.00	173.00	173.00
Min - Max	163.0 - 188.0	140.0 - 185.0	140.0 - 188.0	157.5 - 191.0	147.0 - 193.0	147.0 - 193.0

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=69)	Overall (N=91)	SLT (N=22)	DLT (N=55)	Overall (N=77)
Weight (kg)						
Mean	86.17	85.96	86.01	74.62	77.35	76.57
SD	26.121	21.179	22.318	16.983	17.705	17.435
Median	80.55	83.00	81.60	73.10	77.00	76.20
Min - Max	56.1 - 174.0	53.6 - 171.0	53.6 - 174.0	45.9 - 113.6	42.6 - 141.0	42.6 - 141.0
Primary Cause of Death, n (%)						
Anoxia/Cardiac Arrest	8 (36.4)	29 (42.0)	37 (40.7)	6 (27.3)	18 (32.7)	24 (31.2)
Head Trauma	7 (31.8)	18 (26.1)	25 (27.5)	9 (40.9)	23 (41.8)	32 (41.6)
Cerebrovascular/Stroke	5 (22.7)	20 (29.0)	25 (27.5)	7 (31.8)	12 (21.8)	19 (24.7)
CNS Tumor	1 (4.5)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.8)	1 (1.3)
Other	1 (4.5)	2 (2.9)	3 (3.3)	0 (0.0)	1 (1.8)	1 (1.3)
Age of Death Over 55 Years, n (%)						
Yes	7 (31.8)	6 (8.7)	13 (14.3)	3 (13.6)	4 (7.3)	7 (9.1)
No	15 (68.2)	63 (91.3)	78 (85.7)	19 (86.4)	51 (92.7)	70 (90.9)
Diabetes Diagnosis Status, n (%)						
Yes	4 (18.2)	12 (17.4)	16 (17.6)	0 (0.0)	3 (5.5)	3 (3.9)
No	18 (81.8)	57 (82.6)	75 (82.4)	20 (90.9)	47 (85.5)	67 (87.0)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.1)	3 (5.5)	5 (6.5)
Does the Donor Have a History of Smoking Less Than 20 Pack-Years, n (%)						
Yes	15 (68.2)	47 (68.1)	62 (68.1)	18 (81.8)	32 (58.2)	50 (64.9)
No	4 (18.2)	9 (13.0)	13 (14.3)	0 (0.0)	3 (5.5)	3 (3.9)
Unknown	3 (13.6)	13 (18.8)	16 (17.6)	4 (18.2)	20 (36.4)	24 (31.2)
Chest X-ray Normal Without Infiltrate, n (%)						
Yes	3 (13.6)	14 (20.3)	17 (18.7)	2 (9.1)	18 (32.7)	20 (26.0)
No	19 (86.4)	55 (79.7)	74 (81.3)	19 (86.4)	34 (61.8)	53 (68.8)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	3 (5.5)	4 (5.2)
Bronchoscopy Normal Without Significant Secretions, n (%)						
Yes	8 (36.4)	37 (53.6)	45 (49.5)	12 (54.5)	25 (45.5)	37 (48.1)
No	10 (45.5)	19 (27.5)	29 (31.9)	9 (40.9)	27 (49.1)	36 (46.8)
Unknown	1 (4.5)	2 (2.9)	3 (3.3)	1 (4.5)	3 (5.5)	4 (5.2)
Not Done	3 (13.6)	11 (15.9)	14 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=69)	Overall (N=91)	SLT (N=22)	DLT (N=55)	Overall (N=77)
Sputum Gram Stain Absent of Organisms, n (%)						
Yes	4 (18.2)	15 (21.7)	19 (20.9)	5 (22.7)	10 (18.2)	15 (19.5)
No	4 (18.2)	20 (29.0)	24 (26.4)	7 (31.8)	23 (41.8)	30 (39.0)
Unknown	6 (27.3)	16 (23.2)	22 (24.2)	1 (4.5)	11 (20.0)	12 (15.6)
Not Done	8 (36.4)	18 (26.1)	26 (28.6)	9 (40.9)	11 (20.0)	20 (26.0)
Final PaO_2/FiO_2 Ratio Less Than 300 mmHg, n (%)						
Yes	2 (9.1)	9 (13.0)	11 (12.1)	1 (4.5)	1 (1.8)	2 (2.6)
No	20 (90.9)	60 (87.0)	80 (87.9)	21 (95.5)	54 (98.2)	75 (97.4)

Organ Preservation Times

For non-EVLP recipients, total preservation time (TPT) of each transplanted lung was comprised of a single cold ischemic time period (CIT-1) that spanned the period from donor aortic cross-clamping until initiation of an anastomosis within the recipient's chest cavity; SLT accordingly had one CIT-1, and DLT had two CIT-1s.

For EVLP recipients, TPT of each transplanted lung was comprised of three distinct time periods: CIT-1 (time between donor aortic cross-clamping and initiation of device EVLP); a normothermic EVLP time (time between EVLP initiation and cessation); and a second cold ischemic time (CIT-2) that spanned the time from EVLP cessation until initiation of an anastomosis within the recipient's chest cavity after organ transport with cold static storage preservation. EVLP SLT had one CIT-1, one EVLP time, and one CIT-2, while EVLP DLT had one CIT-1, one EVLP time, and two CIT-2s.

The protocol stipulated that TPT for SLT and first lung of DLT be ≤22 hours; and that TPT for second lung of DLT be ≤26 hours. The breakdown of TPT is below

- EVLP time ≥3 hours but ≤6 hours
- CIT-1 ≤10 hours
- First lung CIT-2 ≤6 hours
- Second lung CIT-2 be 10 hours

Table 12 and Table 13 show the preservation times for recipients' allografts in the Ancillary Population Set and the Matched Analysis Set, respectively. For APS, in the EVLP group, overall median TPT for first lung was 13.11 hours (range: 7.8 to 18.4), and overall median TPT for second lung was 15 hours (range: 8.1 to 20.1). In the non-EVLP group, overall median TPT for first lung was 3.08 hours (range: 1.0 to 7.6), and overall median TPT for second lung was 4.90 hours (range: 1.0 to 9.3). As expected, TPT was markedly longer (mean and median ~10 hours longer) for EVLP than for non-EVLP, which had mean and median cold ischemic times of approximately 3.5 hours (first lung) and 5 hours (second lung). Most of the increased preservation time with EVLP as

compared to non-EVLP was secondary to the need for two separate periods of cold static preservation; EVLP perfusion time was fairly consistent, at approximately 4 hours. Scatter plots of EVLP and non-EVLP subjects' key preservation times are shown in Figure 4 and Figure 5. Ancillary analyses of endpoints stratified by preservation times were performed (see below).

Table 12 Summary of Total Preservation Time - Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
TPT First Lung (Hours)						
Mean	13.16	13.12	13.13	3.35	3.36	3.36
SD	1.807	2.447	2.285	1.208	1.208	1.200
Median	13.13	13.08	13.11	3.10	3.05	3.08
Min - Max	10.6 - 18.2	7.8 - 18.4	7.8 - 18.4	1.1 - 5.9	1.0 - 7.6	1.0 - 7.6
n	25	69	94	23	55	78
TPT Second Lung (Hours)						
Mean		14.55	14.55		4.89	4.89
SD		2.896	2.896		1.591	1.591
Median		15.00	15.00		4.90	4.90
Min - Max		8.1 - 20.1	8.1 - 20.1		1.0 - 9.3	1.0 - 9.3
n		69	69		55	55
CIT-1 (Hours)						
Mean	5.39	5.51	5.48			
SD	1.226	1.601	1.505			
Median	5.17	5.37	5.30			
Min - Max	3.7 - 8.8	2.4 - 9.7	2.4 - 9.7			
n	25	69	94			
EVLP Time (Hours)						
Mean	3.89	3.86	3.87			
SD	0.520	0.350	0.400			
Median	3.68	3.80	3.79			
Min - Max	3.4 - 5.4	3.4 - 5.4	3.4 - 5.4			
n	25	69	94			

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
CIT-2 First Lung (Hours)						
Mean	3.89	3.75	3.78			
SD	1.649	1.328	1.413			
Median	3.90	3.92	3.92			
Min - Max	1.3 - 9.3	1.2 - 6.1	1.2 - 9.3			
n	25	69	94			
CIT-2 Second Lung (Hours)						
Mean		5.17	5.17			
SD		1.919	1.919			
Median		5.65	5.65			
Min - Max		1.4 - 8.3	1.4 - 8.3			
n		69	69			

Table 13: Summary of Total Preservation Time – Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
TPT First Lung (Hours)						
Mean	13.18	13.33	13.29	3.25	3.36	3.33
SD	1.859	2.307	2.181	1.127	1.208	1.179
Median	13.02	13.60	13.28	3.08	3.05	3.07
Min - Max	10.6 - 18.2	8.1 - 18.4	8.1 - 18.4	1.1 - 5.9	1.0 - 7.6	1.0 - 7.6
n	22	57	79	22	55	77
TPT Second Lung (Hours)						
Mean		14.76	14.76		4.89	4.89
SD		2.703	2.703		1.591	1.591
Median		15.25	15.25		4.90	4.90
Min - Max		8.7 - 20.1	8.7 - 20.1		1.0 - 9.3	1.0 - 9.3
n		57	57		55	55
CIT-1 (Hours)						
Mean	5.49	5.62	5.59			
SD	1.249	1.591	1.497			
Median	5.24	5.53	5.45			
Min - Max	3.9 - 8.8	2.5 - 9.7	2.5 - 9.7			
n	22	57	79			
EVLP Time (Hours)						
Mean	3.83	3.89	3.87			
SD	0.437	0.357	0.379			
Median	3.67	3.82	3.82			
Min - Max	3.4 - 5.1	3.4 - 5.4	3.4 - 5.4			
n	22	57	79			

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
CIT-2 First Lung (Hours)						
Mean	3.87	3.82	3.83			
SD	1.739	1.275	1.408			
Median	4.01	4.20	4.12			
Min - Max	1.3 - 9.3	1.4 - 5.7	1.3 - 9.3			
n	22	57	79			
CIT-2 Second Lung (Hours)						
Mean		5.25	5.25			
SD		1.881	1.881			
Median		5.73	5.73			
Min - Max		1.4 - 8.3	1.4 - 8.3			
n		57	57			

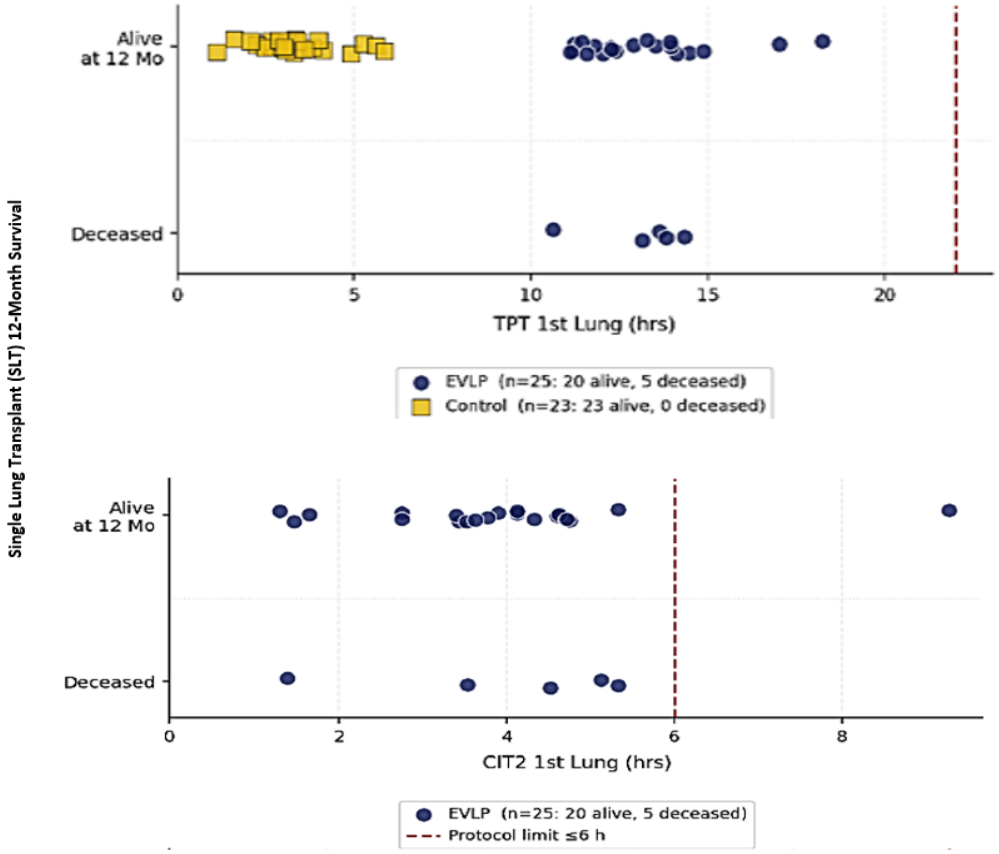


Figure 4 Preservation Times and 12-month Mortality of Single Lung Transplant, EVLP and non-EVLP (Ancillary Population Set)

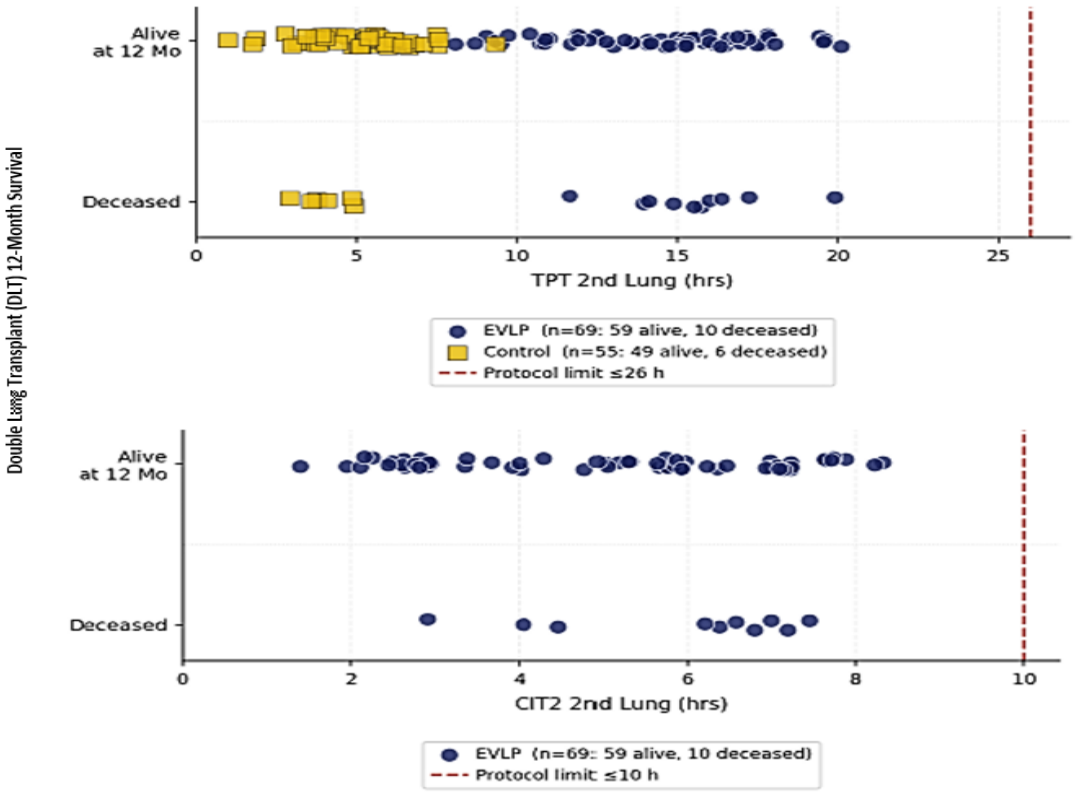


Figure 5 Preservation Times and 12-month Mortality of Double Lung Transplant, EVLP and non-EVLP (Ancillary Population Set)

D. Safety and Effectiveness Results

1. Primary Endpoint – 12-Month Survival Rate Post-Transplant

The Primary Endpoint of the pivotal study was 12-month survival in the setting of index hospitalization discharge by 12-months after transplantation among the combined SLT and DLT EVLP subjects (Full Analysis Set, n=94). All FAS subjects completed the 12-month follow-up assessment of survival, and thus no missing subject primary endpoint survival data required imputation. Table 14 presents the summary of EVLP FAS survival at 12 months. Of the 94 subjects, 79 (84.0%; 95% confidence interval (CI): 75.0%, 90.8%). were alive at 12 months, with all surviving subjects having had index hospitalization discharge before 12 months.

Table 14: Summary of Primary Endpoint: 12-Month Survival – Full Analysis Set

Category	EVLP		
	SLT N=25	DLT N=69	Overall N=94
12 Month Survival or Freedom From Mortality, n (%)			

Category	EVLP		
	SLT N=25	DLT N=69	Overall N=94
Yes	20 (80.0)	59 (85.5)	79 (84.0)
No	5 (20.0)	10 (14.5)	15 (16.0)
95% CI[a]	(59.3, 93.2)	(75.0, 92.8)	(75.0, 90.8)

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Exact binomial was used to construct CIs. The 95% CI was constructed around the proportion of subjects with 12-month survival and prior to initial hospital discharge.

Hypothesis-testing of Primary Endpoint

A Bayesian analysis of the Primary Endpoint was pre-specified. The primary statistical hypothesis was that the posterior probability of the EVLP 12-month survival rate exceeding the performance goal of 81.2% would be greater than 95%. The result of this Bayesian analysis is shown in Table 15. The posterior mean 12-month survival rate was estimated to be 84.3% with a 95% credible interval of 78.9% to 89.0%. The posterior probability that the true 12-month survival rate exceeded the performance goal of 81.2% was 88%. Since this probability was below the pre-specified threshold of 95%, the trial failed to meet its primary endpoint.

Table 15: Bayesian Analysis of Primary Endpoint - Full Analysis Set

	Overall EVLP (N=94)
Posterior Mean	84.3%
95% Credible Interval	(78.9%, 89.0%)
Posterior probability of 12 Month survival rate greater than 81.2%	88%

Primary Endpoint: Comparison of EVLP and non-EVLP

Descriptive comparison of EVLP and non-EVLP 12-month survival was pre-specified, without a statistical hypothesis. The results are shown in Table 16 (APS) and Table 17 (MAS). In both analysis populations, the observed rate of 12-month survival after transplantation was higher among non-EVLP subjects. This trend was most evident in the subgroup of SLT, in which non-EVLP subjects experienced no mortality.

Table 16: 12-Month Survival, EVLP and non-EVLP (Ancillary Population Set)

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
12 Month Survival or Freedom From Mortality, n (%)						
Yes	20 (80.0)	59 (85.5)	79 (84.0)	23 (100)	51 (89.5)	74 (92.5)
No	5 (20.0)	10 (14.5)	15 (16.0)	0 (0.0)	6 (10.5)	6 (7.5)
95% CI[a]	(59.3, 93.2)	(75.0, 92.8)	(75.0, 90.8)	(85.2, 100)	(78.5, 96.0)	(84.4, 97.2)

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Exact binomial was used to construct CIs. The 95% CI was constructed around the proportion of subjects with 12-month survival and prior to initial hospital discharge.

Table 17: 12-Month Survival, EVLP and non-EVLP (Matched Analysis Set)

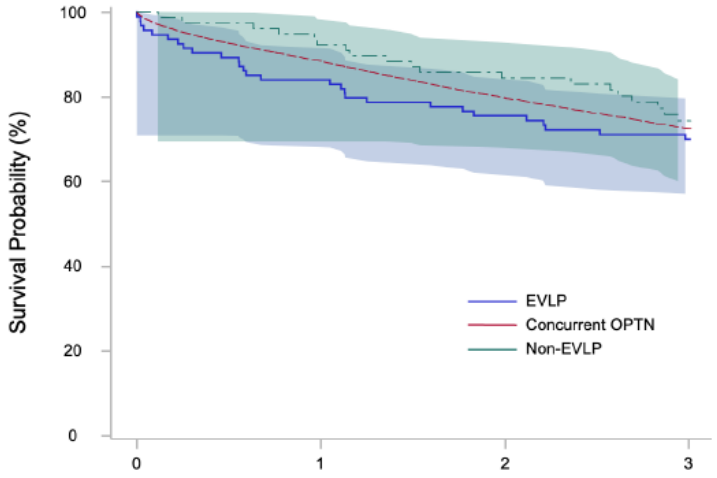
Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
12 Month Survival or Freedom From Mortality, n (%)						
Yes	19 (86.4)	49 (86.0)	68 (86.1)	22 (100)	51 (89.5)	73 (92.4)
No	3 (13.6)	8 (14.0)	11 (13.9)	0 (0.0)	6 (10.5)	6 (7.6)
95% CI[a]	(65.1, 97.1)	(74.2, 93.7)	(76.5, 92.8)	(84.6, 100)	(78.5, 96.0)	(84.2, 97.2)

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Exact binomial was used to construct CIs. The 95% CI was constructed around the proportion of subjects with 12-month survival and prior to initial hospital discharge.

Primary Endpoint: Pre-specified Sub-group Analyses and Adjunctive Longer-term Survival

In addition to evaluating the primary endpoint within the pre-specified SLT and DLT subgroups, analyses of 12-month survival were also conducted for EVLP and, where applicable, non-EVLP donor lungs across other pre-specified baseline covariate subgroups. These results as of March 31, 2025, are presented below in Figure 6, though caution is advised regarding inferences for later time points due to substantial data censoring. At all timepoints, the point estimate of non-EVLP survival is greater than the rate for EVLP subjects. EVLP survival trended lower than that reported by SRTR. For context, aggregate concurrent US survival data from the OPTN/SRTR database are also shown as a *post hoc* comparator.



Treatment Group	Time Point	Procedure	1-year	2-years	3-years
EVLP	# At Risk	93	79	69	57
	# Censored	0	0	2	7
	# Events	1	14	8	5
	Event-free [%]	98.9%	84.0%	75.5%	70.0%
	95% Confidence Interval [%]	92.7%-99.8%	74.9% -90.1%	65.5% -83.0%	59.5% -78.2%
Non-EVLP	# At Risk	78	72	62	43
	# Censored	0	0	4	12

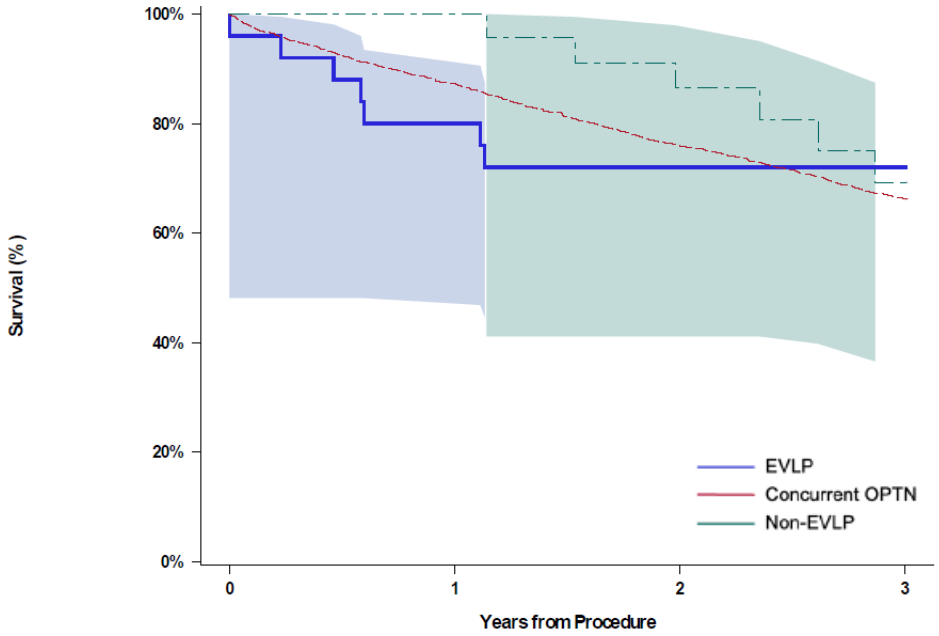
	# Events	0	6	6	7
	Event-free [%]	100.0%	92.3%	84.5%	74.4%
	95% Confidence Interval [%]	N/A	83.7% - 96.5%	74.3% - 90.9%	62.7% - 82.9%
Concurrent OPTN	# At Risk	9331	8204	6577	4142
	# Censored	0	71	818	1934
	# Events	7	1056	809	501
	Event-free [%]	99.9%	88.6%	79.8%	72.5%
	95% Confidence Interval [%]	99.8% - 100.0%	87.9% - 89.2%	78.9% - 80.6%	71.5% - 73.4%

Figure 6: Survival Estimates for EVLP and non-EVLP Subjects (Ancillary Population Set), and OPTN

Transplant Type: SLT or DLT

SLT

EVLP SLT appeared to have an increased mortality risk within the first two post-operative years as compared to non-EVLP SLT, but the survival difference decreased subsequently.



Treatment Group	Transplant Type	Time Point	Procedure	1-year	2-years	3-years
EVLP	SLT	# At Risk	24	20	16	14
		# Censored	0	0	2	2
		# Events	1	4	2	0
		Event-free [%]	96.0%	80.0%	72.0%	72.0%
		95% Confidence Interval [%]	74.8% - 99.4%	58.4% - 91.1%	50.1% - 85.5%	50.1% - 85.5%
Non-EVLP	SLT	# At Risk	23	23	18	12

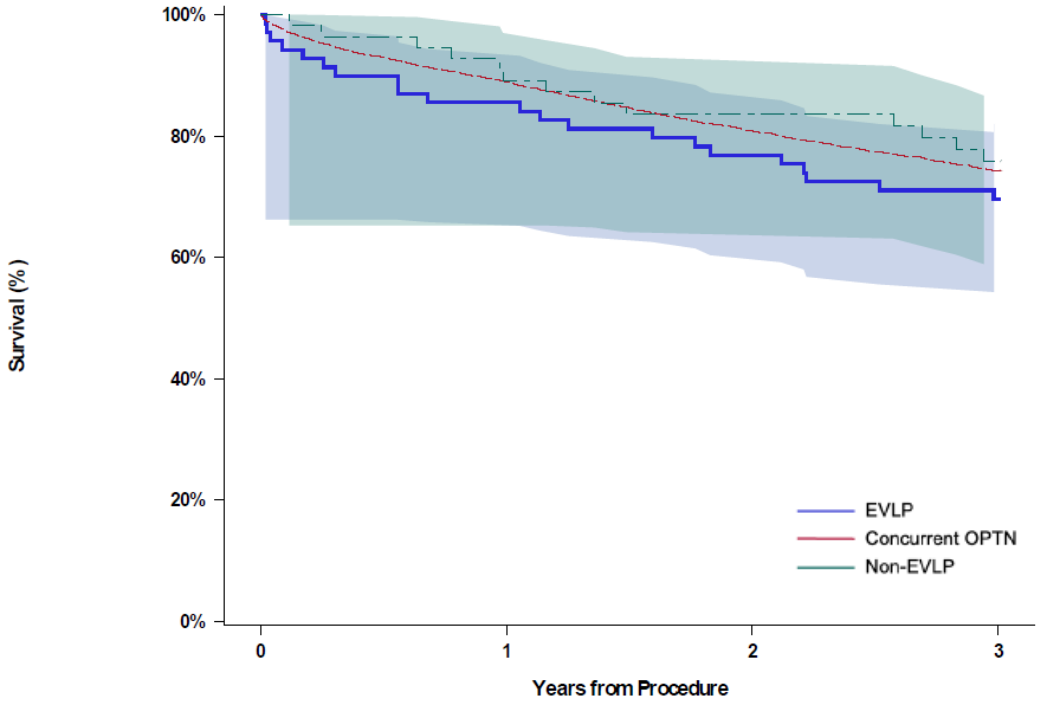
Treatment Group	Transplant Type	Time Point	Procedure	1-year	2-years	3-years
		# Censored	0	0	2	3
		# Events	0	0	3	3
		Event-free [%]	100.0%	100.0%	86.5%	69.2%
		95% Confidence Interval [%]	N/A	N/A	63.8% - 95.5%	43.4% - 85.0%
Concurrent OPTN	SLT	# At Risk	2055	1778	1381	870
		# Censored	0	18	172	360
		# Events	2	259	225	151
		Event-free [%]	99.9%	87.3%	76.1%	66.2%
		95% Confidence Interval [%]	99.6% - 100.0%	85.7% - 88.6%	74.1% -77.9%	64.0% - 68.3%

Abbreviations: EVLO, ex vivo lung perfusion; SLT, single lung transplant

Figure 7: Survival Estimates for Single Lung EVLP and non-EVLP Subjects (Ancillary Population Set), and OPTN

DLT

For DLT, EVLP recipients experienced moderately increased mortality compared to non-EVLP, which persisted beyond 1 year.



Treatment Group	Transplant Type	Time Point	Procedure	1-year	2-years	3-years
EVLP	DLT	# At Risk	69	59	53	43
		# Censored	0	0	0	5
		# Events	0	10	6	5
		Event-free [%]	100.0%	85.5%	76.8%	69.6%

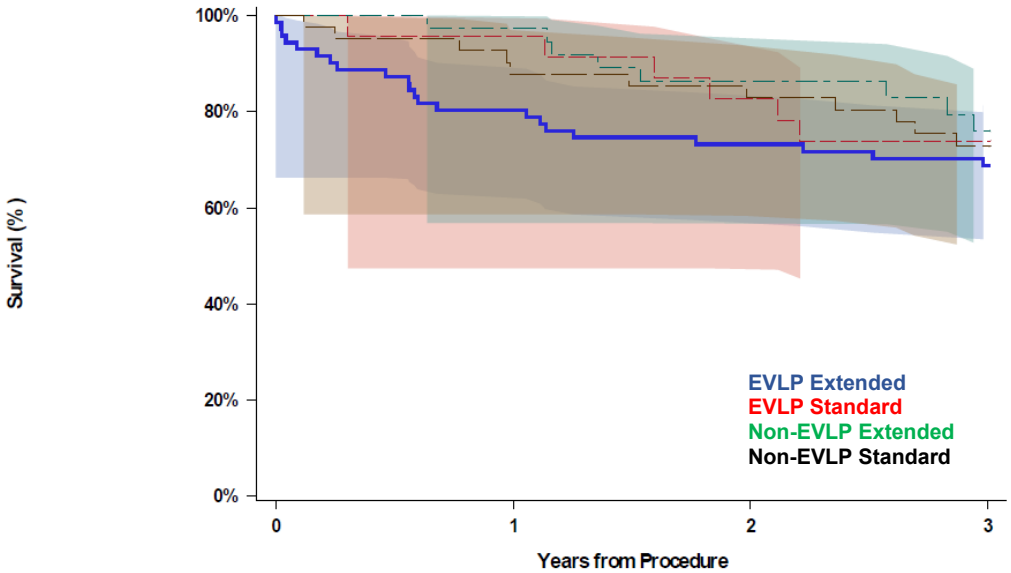
Treatment Group	Transplant Type	Time Point	Procedure	1-year	2-years	3-years
		95% Confidence Interval [%]	N/A	74.7% - 91.9%	65.0% - 85.1%	57.2% - 79.0%
Non-EVLP	DLT	# At Risk	55	49	44	31
		# Censored	0	0	2	9
		# Events	0	6	3	4
		Event-free [%]	100.0%	89.1%	83.6%	75.9%
		95% Confidence Interval [%]	N/A	77.3% - 94.9%	70.8% - 91.1%	62.1% - 85.2%
Concurrent OPTN	DLT	# At Risk	7276	6426	5196	3272
		# Censored	0	53	646	1574
		# Events	5	797	584	350
		Event-free [%]	99.9%	89.0%	80.0%	74.3%
		95% Confidence Interval [%]	99.8% - 100.0%	88.2% - 89.7%	79.9% - 81.7%	73.2% - 75.3%

Abbreviation: DLT, double lung transplant EVLP, ex vivo lung perfusion

Figure 8: Survival Estimates for Double Lung EVLP and non-EVLP Subjects (Ancillary Population Set), and OPTN

Donor Lung Criteria: Standard Criteria or Extended Criteria

Recipients of standard criteria donor lungs had similar survival rates irrespective of preservationm cohort (EVLP versus non-EVLP). However, the observed survival in recipients of EVLP extended criteria donor organs was substantially lower than the other cohorts' survival rates.. A higher proportion of EVLP subjects received extended criteria donor organs, and that difference was driven predominantly by a substantially higher prevalence of DCD donors within the EVLP group (see Figure 9 below).

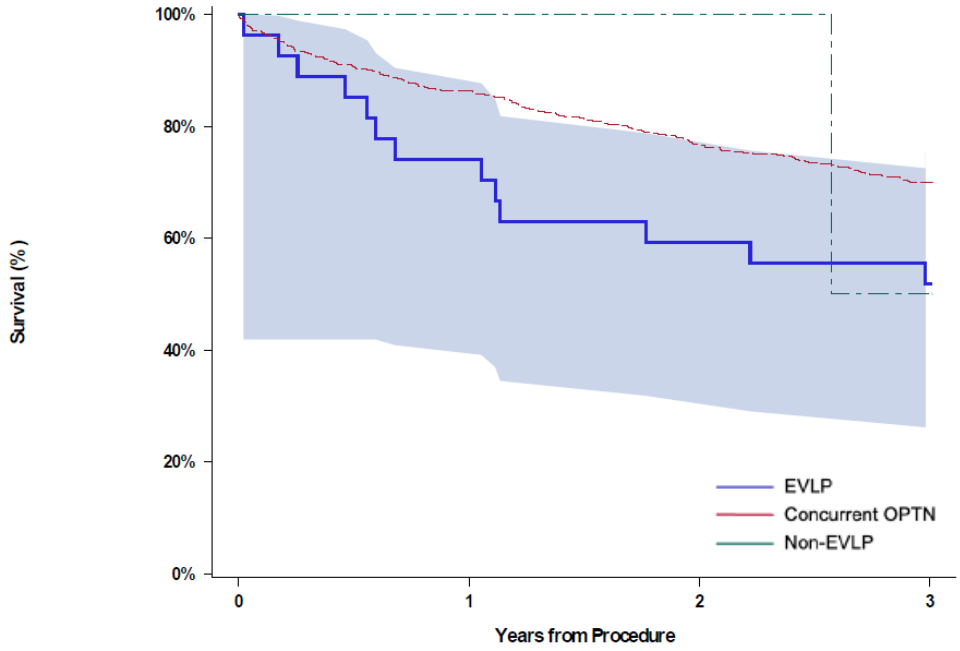


Treatment Group	Standard Donor Lung	Time Point	Procedure	1-year	2-years	3-years
EVLP	Extended Donor Lung	# At Risk	70	57	50	41
		# Censored	0	0	2	6
		# Events	1	13	5	3
		Event-free [%]	98.6%	80.3%	73.2%	68.7%
		95% Confidence Interval [%]	90.4% - 99.8%	69.0% - 87.8%	61.3% - 82.0%	56.5% - 78.2%
	Standard Donor Lung	# At Risk	23	22	19	16
		# Censored	0	0	0	1
		# Events	0	1	3	2
		Event-free [%]	100.0%	95.7%	82.6%	73.9%
		95% Confidence Interval [%]	N/A	72.9% - 99.4%	60.1% - 93.1%	50.9% - 87.3%
Non-EVLP	Extended Donor Lung	# At Risk	37	36	29	18
		# Censored	0	0	3	8
		# Events	0	1	4	3
		Event-free [%]	100.0%	97.3%	86.2%	76.0%
		95% Confidence Interval [%]	N/A	82.3% - 99.6%	70.0% - 94.0%	57.4% - 87.3%
	Standard Donor Lung	# At Risk	41	36	33	25
		# Censored	0	0	1	4
		# Events	0	5	2	4
		Event-free [%]	100.0%	87.8%	82.9%	72.9%
		95% Confidence Interval [%]	N/A	73.2% - 94.7%	67.5% - 91.5%	56.4% - 84.0%

Figure 9: Survival Estimates for Donor Lung Criteria, EVLP and non-EVLP Subjects (Ancillary Population Set)

Donor Donation Type: DCD or DBD

There were only 2 DCD donor organs in the non-EVLP group. The observed DCD survival at 2 years after EVLP (59%) was lower than 2 year survival after DCD as reported by the SRTR (77%).

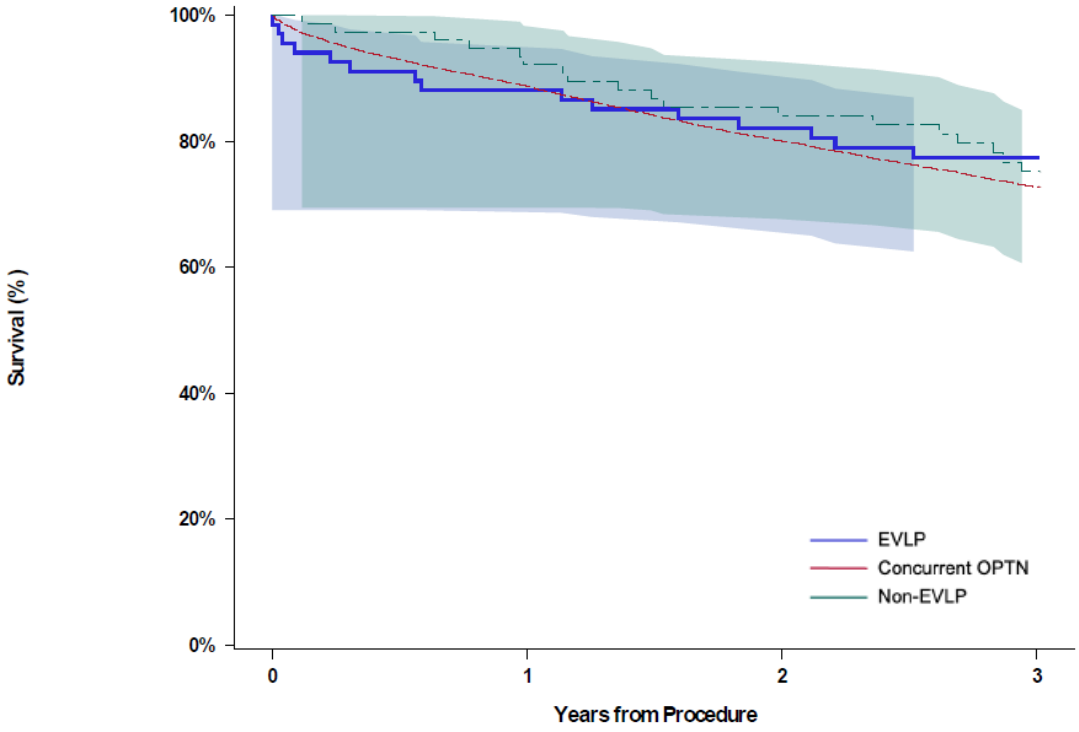


Treatment Group	Standard Donor Lung	Time Point	Procedure	1-year	2-years	3-years
EVLP	DCD	# At Risk	27	20	16	11
		# Censored	0	0	0	3
		# Events	0	7	4	2
		Event-free [%]	100.0%	74.1%	59.3%	51.9%
		95% Confidence Interval [%]	N/A	53.2 – 86.7%	38.6% - 75.0%	31.9% - 68.5%
Non-EVLP	DCD	# At Risk	2	2	2	1
		# Censored	0	0	0	0
		# Events	0	0	0	1
		Event-free [%]	100.0 %	100.0 %	100.0 %	100.0 %
		95% Confidence Interval [%]	N/A	N/A	N/A	0.6%-91.0%
Concurrent OPTN	DCD	# At Risk	665	570	444	263
		# Censored	0	4	63	149
		# Events	0	91	63	32
		Event-free [%]	100.0%	86.3%	76.7%	70.0%
		95% Confidence Interval [%]	N/A	83.4% - 88.7%	73.2% - 79.7%	66.1% - 73.5%

Abbreviations: DCD, donation after circulatory death

Figure 10: Survival Estimates for DCD Donation Type, EVLP and non-EVLP Subjects (Ancillary Population Set), and OPTN

The observed DBD survival rates were similar among the EVLP, non-EVLP, and OPTN cohorts.



Treatment Group	Donor Death Type	Time Point	Procedure	1-year	2-years	3-years
EVLP	DBD	# At Risk	66	59	53	46
		# Censored	0	0	2	4
		# Events	1	7	4	3
		Event-free [%]	98.5%	88.1%	82.1%	77.4%
		95% Confidence Interval [%]	89.9% - 99.8%	77.5% - 93.8%	70.6% - 89.4%	65.3% - 85.7%
Non-EVLP	DBD	# At Risk	76	70	60	42
		# Censored	0	0	4	12
		# Events	0	6	6	6
		Event-free [%]	100.0%	92.1%	84.1%	75.1%
		95% Confidence Interval [%]	N/A	83.3% - 96.4%	73.6% - 90.6%	63.4% - 83.6%
Current OPTN	DBD	# At Risk	8666	7634	6133	3879
		# Censored	0	67	755	1785
		# Events	7	965	746	469
		Event-free [%]	99.9%	88.8%	80.0%	72.7%
		95% Confidence Interval [%]	99.8% - 100%	88.1% - 89.4%	79.1% - 80.0%	71.1% - 73.7%

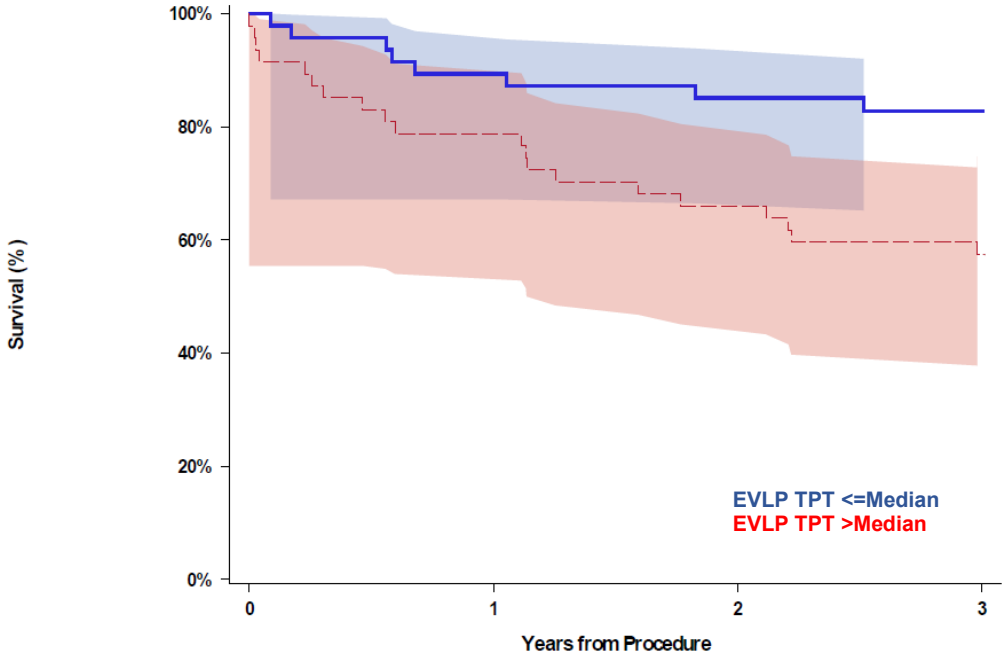
Abbreviations: DBD, donation after brain death

Figure 11: Survival Estimates for DBD Donation Type, EVLP and non-EVLP Subjects (Ancillary Population Set), and OPTN

Total Preservation Time

TPT of EVLP Group

The median total preservation time (TPT) was 13.1 hours for, collectively, EVLP SLT and first lung-DLT. The median TPT for EVLP second lung DLT was 15 hours. EVLP survival survival estimates for the FAS population were stratified by median first-lung TPT (i.e., > 13.1 hours and ≤ 13.1 hours). EVLP TPT greater than the median appeared to be associated with a substantial decrease in survival.



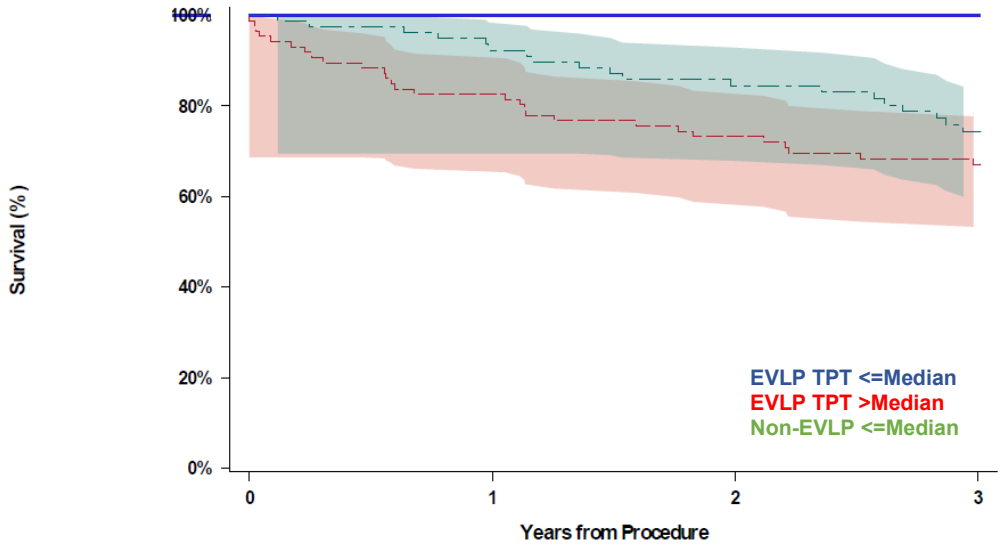
Treatment Group	Total Preservation Time	Time Point	Procedure	1-year	2-years	3-years
EVLP	Total Preservation Time <= Median = 13.11	# At Risk	47	42	38	33
		# Censored	0	0	2	4
		# Events	0	5	2	1
		Event-free [%]	100.0%	89.4%	85.1%	82.8%
		95% Confidence Interval [%]	N/A	76.3% - 95.4%	71.3% - 92.6%	68.5% - 91.0%
	Total Preservation Time > Median = 13.11	# At Risk	46	37	31	24
		# Censored	0	0	0	3
		# Events	1	9	6	4
		Event-free [%]	97.9%	78.7%	66.0%	57.4%
		95% Confidence Interval [%]	85.5% - 99.7%	64.1% - 87.9%	50.5% - 77.6%	42.0% - 70.0%

Figure 12: Survival Estimates for EVLP Subjects, Stratified by Median First Lung Total Preservation Time (Full Analysis Set)

TPT of EVLP and non-EVLP Groups

TPT for non-EVLP transplants was equivalent to CIT-1, the medians of which were 3.1 hours for first lung and 4.9 hours for second lung. For the APS as a whole (i.e., EVLP + non-EVLP donor lungs), the median TPT

was 10.2 hours. The sample size of shorter-duration TPT (<10 hours) among EVLP recipients was small (n=8), and, none of the non-EVLP preservations were >10 hours. Although these sample size differences impose marked limitations for inferences, Kaplan-Meier survival analyses do suggest that TPT longer than the LungFX intended maximum (20 hours) is associated with shorter recipient survival.

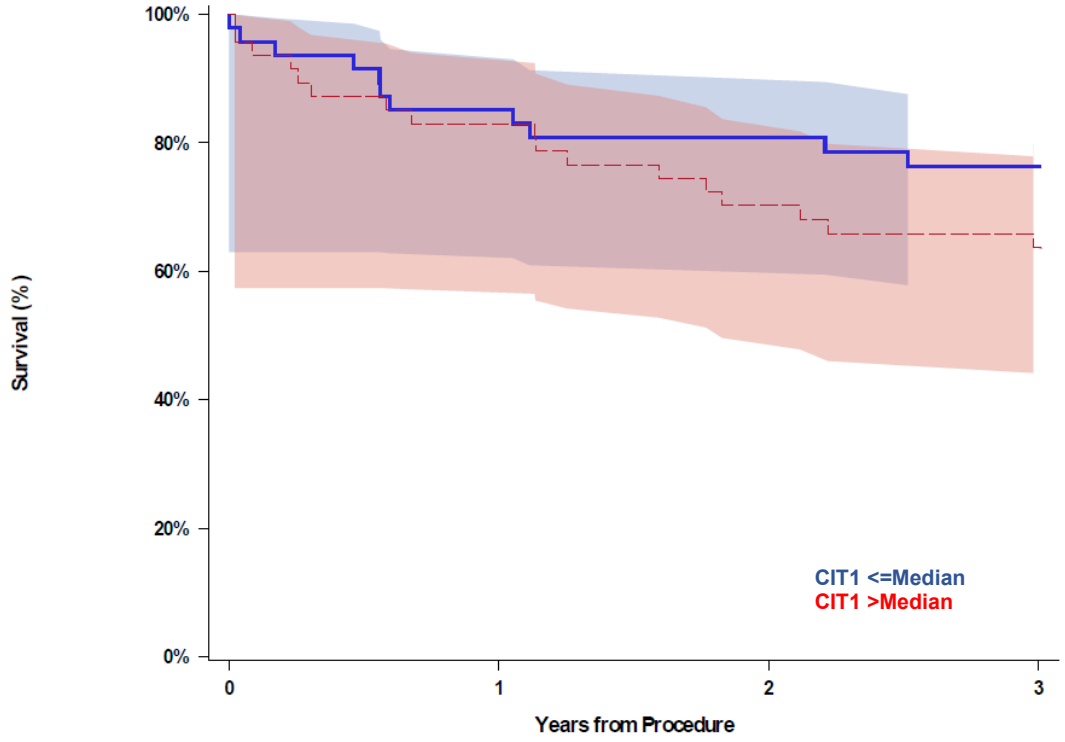


Treatment Group	Total Preservation Time	Time Point	Procedure	1-year	2-years	3-years
EVLP	Total Preservation Time <= Median = 10.22	# At Risk	8	8	8	7
		# Censored	0	0	0	1
		# Events	0	0	0	0
		Event-free [%]	100.0%	100.0%	100.0%	100.0%
		95% Confidence Interval [%]	N/A	N/A	N/A	N/A
	Total Preservation Time > Median = 10.22	# At Risk	85	71	61	50
		# Censored	0	0	2	6
		# Events	1	14	8	5
		Event-free [%]	98.8%	82.6%	73.3%	67.1%
		95% Confidence Interval [%]	92.0%-99.8%	72.7% - 89.1%	62.6% - 81.3%	56.0% - 76.0%
Non-EVLP	Total Preservation Time <= Median = 10.22	# At Risk	78	72	62	43
		# Censored	0	0	4	12
		# Events	0	6	6	7
		Event-free [%]	100.0%	92.3%	84.5%	74.4%
		95% Confidence Interval [%]	N/A	83.7% - 96.5%	74.3% - 90.9%	62.7% - 82.9%

Figure 13: Survival Estimates for EVLP and non-EVLP Subjects, Stratified by Median First Lung Total Preservation Time (Ancillary Population Set)

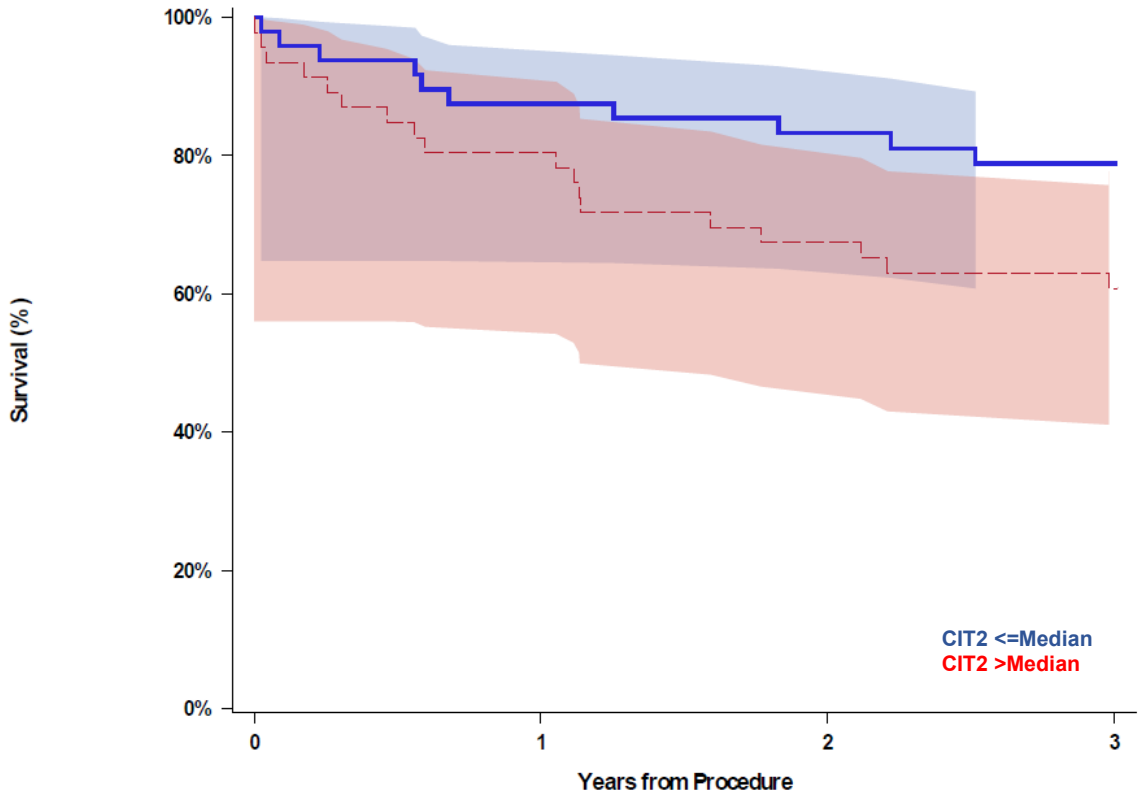
EVLP Cold Ischemic Times

EVLP survival stratified by first lung median cold ischemic times (5.3 hours (CIT-1), 3.9 hours (CIT-2)) are shown below in Figure 14 and Figure 15, respectively. Longer term survival appears to be associated with shorter durations of the two cold ischemic preservation periods required for a completed LungFX EVLP procedure. Importantly, EVLP DLT accrued a second CIT-2 as compared to SLT, and thus interpretation of the presented stratification could be confounded by any influence that the longer second lungs' CIT-2 may have on survival estimates.



Cold Ischemic Time 1	Time Point	Procedure	1-year	2-years	3-years
CIT1 <= Median = 5.3	# At Risk	46	40	37	30
	# Censored	0	0	1	5
	# Events	1	6	2	2
	Event-free [%]	97%	85.1%	80.9%	76.4%
	95% Confidence Interval [%]	85.8% - 99.7%	71.3% - 92.6%	66.4% - 89.5%	61.4% - 86.2%
CIT1 > Median = 5.3	# At Risk	47	39	32	27
	# Censored	0	0	1	2
	# Events	0	8	6	3
	Event-free [%]	100.0%	83.0%	70.2%	63.6%
	95% Confidence Interval [%]	N/A	68.8% - 91.1%	55.0% - 81.1%	48.2% - 75.6%

Figure 14: Survival Estimates for EVLP and non-EVLP Subjects, Stratified by Median First Lung Total Preservation Time (Ancillary Population Set)



Cold Ischemic Time 2	Time Point	Procedure	1-year	2-years	3-years
CIT2 <= Median = 3.92	# At Risk	48	42	38	32
	# Censored	0	0	2	4
	# Events	0	6	2	2
	Event-free [%]	100.0%	87.5%	83.3%	78.8%
	95% Confidence Interval [%]	N/A	74.3% - 94.2%	69.4% - 91.3%	64.2% - 88.0%
CIT2 > Median = 3.92	# At Risk	45	37	31	25
	# Censored	0	0	0	3
	# Events	1	8	6	3
	Event-free [%]	97.8%	80.4%	67.4%	60.8%
	95% Confidence Interval [%]	85.6% - 99.7%	65.8% - 89.3%	51.9% - 78.9%	45.2% - 73.2%

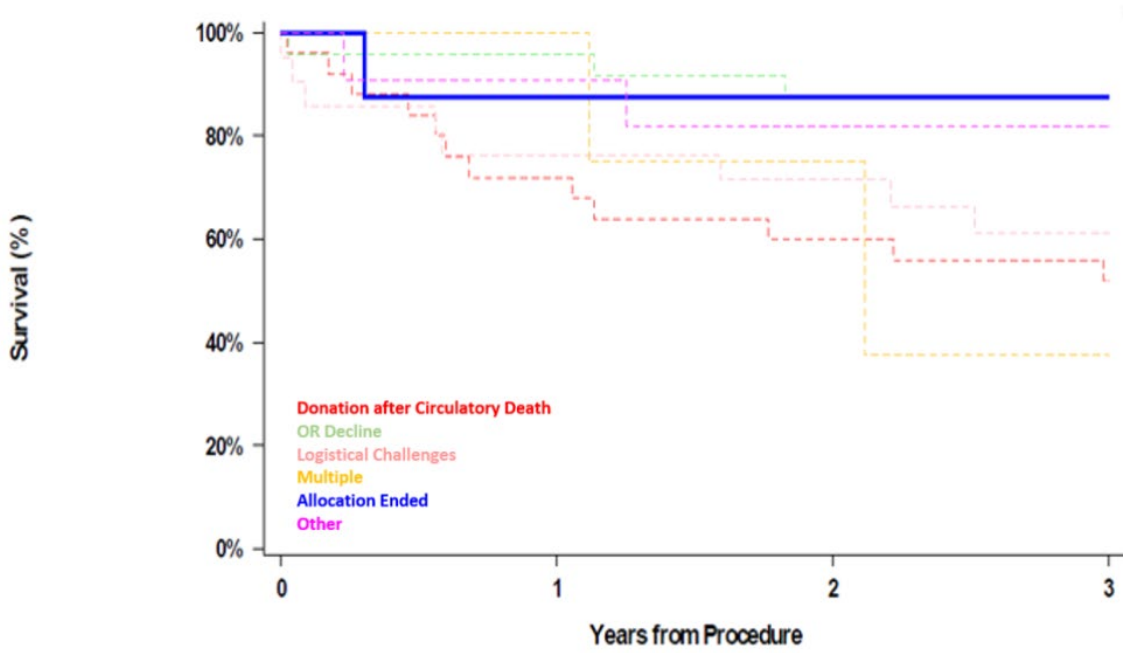
Figure 15: Survival Estimates for EVLP Subjects, Stratified by Median First Lung Cold Ischemic Time-2 (Full Analysis Set)

Other Sub-groups Survival Analyses

Additional pre-specified subgroup analyses included study site enrollement (high-enrolling versus low-enrolling), donor lung referral source (transplant center versus OPO), and use of ECMO pre-operatively (few study subjects in either arm were being treated with ECMO pre-operatively). No clinically meaningful differences in longer-term survival were noted within these sub-groups.

Survival by EVLP Referral Reason (*post hoc)*

The justification for each EVLP referral was prospectively collected by OPOs (see Table 10 above). A post hoc survival analysis stratified by EVLP referral reason is shown below. The number of recipients in each subgroup was small, but DCD, intra-operative decline, and presence of "logistical challenges" were the most frequent reasons cited (28%, 27%, and 25%, respectively). Among them, DCD and logistical challenges were associated with substantially lower longer-term survival than what was observed for DBD organs referred because of intra-operative decline of recipient-matched donor lungs.



Referral Reasons	Time Point	Procedure	1-year	2-years	3-years
Donation after Circulatory Death	# At Risk	25	18	15	11
	# Censored	0	0	0	2
	# Events	0	7	3	2
	Event-free [%]	100.0%	72.0%	60.0%	52.0%
	95% Confidence Interval [%]	N/A	50.1% - 85.5%	38.4% - 76.1%	31.2% - 69.2%
OR Decline	# At Risk	24	23	21	20
	# Censored	0	0	0	1
	# Events	0	1	2	0
	Event-free [%]	100.0%	95.8%	87.5%	87.5%
	95% Confidence Interval [%]	N/A	73.9% - 99.4%	66.1% - 95.8%	66.1% - 95.8%
	Greenwood SE [%]	0.0%	4.1%	6.8%	6.8%
Logistical Challenges	# At Risk	20	16	14	11
	# Censored	0	0	1	1
	# Events	1	4	1	2
	Event-free [%]	95.2%	76.2%	71.4%	61.2%
	95% Confidence Interval [%]	70.7% - 99.3%	51.9% - 89.3%	47.2% - 86.0%	37.1% - 78.4%
Multiple	# At Risk	4	4	2	1
	# Censored	0	0	1	0
	# Events	0	0	1	1
	Event-free [%]	100.0%	100.0%	75.0%	37.5%
	95% Confidence Interval [%]	N/A	N/A	12.8% - 96.1%	1.1% - 80.8%
Allocation Ended	# At Risk	8	7	7	6
	# Censored	0	0	0	1
	# Events	0	1	0	0
	Event-free [%]	100.0%	87.5%	87.5%	87.5%
	95% Confidence Interval [%]	N/A	38.7% - 98.1%	38.7% - 98.1%	38.7% - 98.1%
Other	# At Risk	11	10	9	7
	# Censored	0	0	0	2
	# Events	0	1	1	0
	Event-free [%]	100.0%	90.9%	81.8%	81.8%
	95% Confidence Interval [%]	N/A	50.8% - 98.7%	44.7% - 95.1%	44.7% - 95.1%

Figure 16: Survival Estimates for EVLP Subjects, Stratified by Referral Reason (Full Analysis Set, *post hoc*)

2. Secondary Endpoints

2.1 Survival through 12 Months

Of the 94 EVLP-evaluated lung transplant recipients, 79 (84.0%) were free from mortality at 12 months (20 SLT and 59 DLT). Of the 80 non-EVLP lung transplant recipients, 74 (92.5%) were free from mortality at 12 months (23 SLT and 51 DLT). Mortality was higher in EVLP at all time points from the time of transplantation through 12 months. No subjects experienced graft failure

leading to re-transplantation during the 12-month post-transplantation period (Table 18).

Similar results were observed in the Matched Analysis Set (Table 19)

Table 18: Summary of Subject Survival - Ancillary Population Set

Timepoint Subject Status	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
Day 30 Post-transplant, n (%)						
Alive	24 (96.0)	66 (95.7)	90 (95.7)	23 (100)	57 (100)	80 (100)
Deceased	1 (4.0)	3 (4.3)	4 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)
95% CI[a]	(79.6, 99.9)	(87.8, 99.1)	(89.5, 98.8)	(85.2, 100.0)	(93.7, 100.0)	(95.5, 100.0)
Day 90 Post-transplant, n (%)						
Alive	23 (92.0)	64 (92.8)	87 (92.6)	23 (100)	56 (98.2)	79 (98.8)
Deceased	2 (8.0)	5 (7.2)	7 (7.4)	0 (0.0)	1 (1.8)	1 (1.3)
95% CI[a]	(74.0, 99.0)	(83.9, 97.6)	(85.3, 97.0)	(85.2, 100.0)	(90.6, 100.0)	(93.2, 100.0)
Month 6 Post-transplant, n (%)						
Alive	22 (88.0)	62 (89.9)	84 (89.4)	23 (100)	55 (96.5)	78 (97.5)
Deceased	3 (12.0)	7 (10.1)	10 (10.6)	0 (0.0)	2 (3.5)	2 (2.5)
95% CI[a]	(68.8, 97.5)	(80.2, 95.8)	(81.3, 94.8)	(85.2, 100.0)	(87.9, 99.6)	(91.3, 99.7)
Month 12 Post-transplant, n(%)						
Alive	20 (80.0)	59 (85.5)	79 (84.0)	23 (100)	51 (89.5)	74 (92.5)
Deceased	5 (20.0)	10 (14.5)	15 (16.0)	0 (0.0)	6 (10.5)	6 (7.5)
95% CT[a]	(59.3, 93.2)	(75.0, 92.8)	(75.0, 90.8)	(85.2, 100.0)	(78.5, 96.0)	(84.4, 97.2)

a Exact binomial was used to construct confidence intervals

Table 19: Summary of Subject Survival - Matched Analysis Set

Timepoint Subject Status	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Day 30 Post-transplant, n (%)						
Alive	21 (95.5)	55 (96.5)	76 (96.2)	22 (100)	57 (100)	79 (100)
Deceased	1 (4.5)	2 (3.5)	3 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
95% CI[a]	(77.2, 99.9)	(87.9, 99.6)	(89.3, 99.2)	(84.6, 100.0)	(93.7, 100.0)	(95.4, 100.0)
Day 90 Post-transplant, n (%)						
Alive	21 (95.5)	53 (93.0)	74 (93.7)	22 (100)	56 (98.2)	78 (98.7)
Deceased	1 (4.5)	4 (7.0)	5 (6.3)	0 (0.0)	1 (1.8)	1 (1.3)
95% CI[a]	(77.2, 99.9)	(83.0, 98.1)	(85.8, 97.9)	(84.6, 100.0)	(90.6, 100.0)	(93.1, 100.0)
Month 6 Post-transplant, n (%)						
Alive	21 (95.5)	51 (89.5)	72 (91.1)	22 (100)	55 (96.5)	77 (97.5)
Deceased	1 (4.5)	6 (10.5)	7 (8.9)	0 (0.0)	2 (3.5)	2 (2.5)
95% CI[a]	(77.2, 99.9)	(78.5, 96.0)	(82.6, 96.4)	(84.6, 100.0)	(87.9, 99.6)	(91.2, 99.7)
Month 12 Post-transplant, n(%)						
Alive	19 (86.4)	49 (86.0)	68 (86.1)	22 (100)	51 (89.5)	73 (92.4)
Deceased	3 (13.6)	8 (14.0)	11 (13.9)	0 (0.0)	6 (10.5)	6 (7.6)

Timepoint Subject Status	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
95% CI[a]	(65.1, 97.1)	(74.2, 93.7)	(76.5, 92.8)	(84.6, 100.0)	(78.5, 96.0)	(84.2, 97.2)
95% CI[a]	(65.1, 97.1)	(74.2, 93.7)	(76.5, 92.8)	(84.6, 100.0)	(78.5, 96.0)	(84.2, 97.2)

a Exact binomial was used to construct Confidence Intervals (CI)

Overall, there were 24 deaths in the APS that occurred during the study's period of prospective data collection, 17 deaths in the EVLP group (range: 1 to 415 days post-transplant) and 7 deaths in the non-EVLP group (range: 43 to417 days post-transplant). Of those 24 deaths, 21 occurred during the 12-month Post-Intervention Period, 15 in the EVLP group and 6 in the non-EVLP group.

Table 20: Summary of Deaths During 12-month Post-Intervention Period - All Subjects

Group (Subgroup)	Primary Cause of Death as Reported	Days Survived Following Transplant
EVLP (SLT)	Cardiovascular arrest death[a]	169
EVLP (SLT)	Myocardial infarction	218
EVLP (SLT)	Multiorgan failure due to sepsis	83
EVLP (SLT)	Intraoperative hemorrhage	1
EVLP (SLT)	Graft failure[a]	213
EVLP (DLT)	Complications of CVA with hemorrhagic conversion	63
EVLP (DLT)	Cardiorespiratory arrest due to probable airway obstruction (due to mucus plug)	111
EVLP (DLT)	COVID-19 virus infection	204
EVLP (DLT)	Septic shock	94
EVLP (DLT)	Hypoxemic and hypercapnic respiratory failure, shock[a,b]	15
EVLP (DLT)	Adenoviral pneumonia complicating primary graft dysfunction[a]	32
EVLP (DLT)	Signet ring cell adenocarcinoma of unknown primary	205
EVLP (DLT)	Heart failure[b]	8
EVLP (DLT)	Allograft failure, per Pulmonologist	248
EVLP (DLT)	Hyperammonemia	9
Non-EVLP (DLT)	Respiratory failure due to adenovirus pneumonia. Other contributing factors: renal failure, severe malnutrition, probable septic shock	91
Non-EVLP (DLT)	Massive hemoptysis	43
Non-EVLP (DLT)	Acute myelogenous leukemia	233
Non-EVLP (DLT)	Anoxic brain injury	283
Non-EVLP (DLT)	Severe sepsis due to Acinetobacter and vancomycin-resistant enterococcus pneumonia	360
Non-EVLP (DLT)	Septic shock	354

Abbreviations: AE, adverse event; CEC, Clinical Events Committee; COVID, coronavirus disease; CVA, cerebrovascular accident; DLT, double lung transplant; EVLP, ex vivo lung perfusion; MedDRA, Medical Dictionary for Regulatory Activities; SLT, single lung transplant

a Possibly related to EVLP by the CEC.

b Possibly related to EVLP by the Investigator. Note: Vital status was assessed at each study visit.

2.2 Adjudicated Lung Graft-related Mortality

For all fatal events during prospective study follow-up, the CEC adjudicated whether death was directly or indirectly related to either lung graft failure or other graft-related complications. The CEC further adjudicated the relatedness of reported serious adverse events (SAEs) to EVLP, the transplant procedure, and/or post-transplantation ECMO use.

Of the 15 EVLP deaths within 12 months:

- 10 (3 SLT and 7 DLT) were adjudicated as related to the lung graft
- 10 (2 SLT and 8 DLT) were adjudicated as related to the lung transplant procedure.

The CEC further assessed 4 of the 15 deaths as having been possibly related to EVLP.

Of the 6 non-EVLP deaths within 12 months:

- 5 (5 DLT) were adjudicated as related to the lung graft
- 6 (6 DLT) were adjudicated as related to the lung transplant procedure.

Table 21 presents a summary of all 12-months deaths' adjudicated relatedness to the lung transplant procedure and the lung graft. Compared to non-EVLP recipients, EVLP recipients experienced proportionately more lung graft-related mortality (11% versus 6%) and more lung transplant procedure-related mortality (11% versus 8%), though, as noted above, when mortality did occur, it was more frequently related to the lung transplant procedure and graft in non-EVLP subjects than in EVLP subjects.

Table 21: Summary of 12-Month Mortality Adjudicated by CEC - Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
Related to Lung Graft by CEC, n (%)						
Yes	3 (12.0)	7 (10.1)	10 (10.6)	0 (0.0)	5 (8.8)	5 (6.3)
No	2 (8.0)	3 (4.3)	5 (5.3)	0 (0.0)	1 (1.8)	1 (1.3)
95% CI[a]	(2.5, 31.2)	(4.2, 19.8)	(5.2, 18.7)	(0.0, 14.8)	(2.9, 19.3)	(2.1, 14.0)
Related to Lung Transplant Procedure by CEC, n (%)						
Yes	2 (8.0)	8 (11.6)	10 (10.6)	0 (0.0)	6 (10.5)	6 (7.5)
No	3 (12.0)	2 (2.9)	5 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)
95% CI[b]	(1.0, 26.0)	(5.1, 21.6)	(5.2, 18.7)	(0.0, 14.8)	(4.0, 21.5)	(2.8, 15.6)

Abbreviations: CEC, Clinical Events Committee; CI, confidence interval; DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Exact binomial was used to construct CIs. The 95% CI was constructed around the proportion of subjects with 12-month mortality related to lung graft.

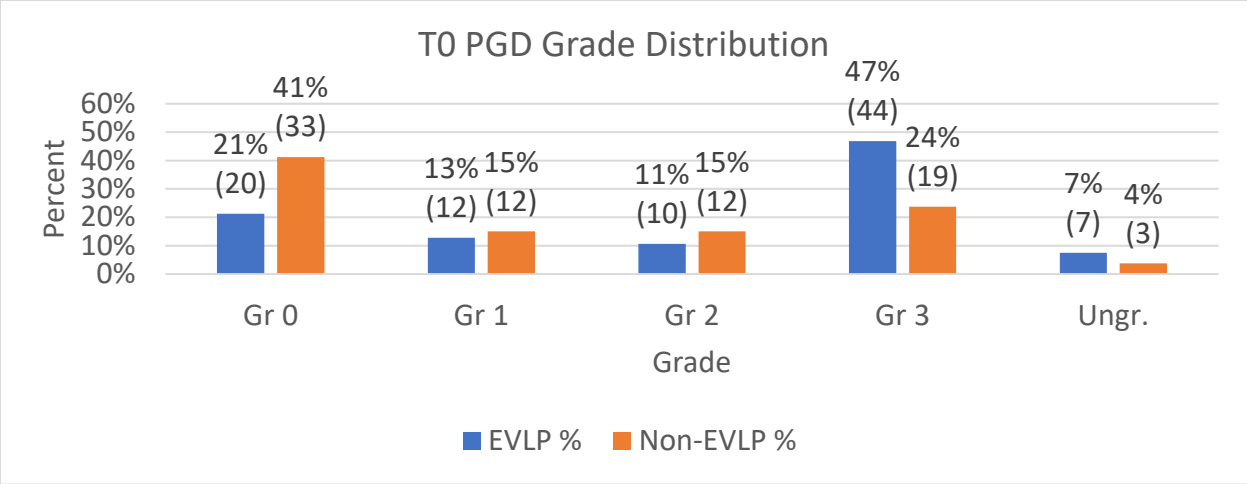
b Exact binomial was used to construct CIs. The 95% CI was constructed around the proportion of subjects with 12-month mortality related to lung transplant procedure.

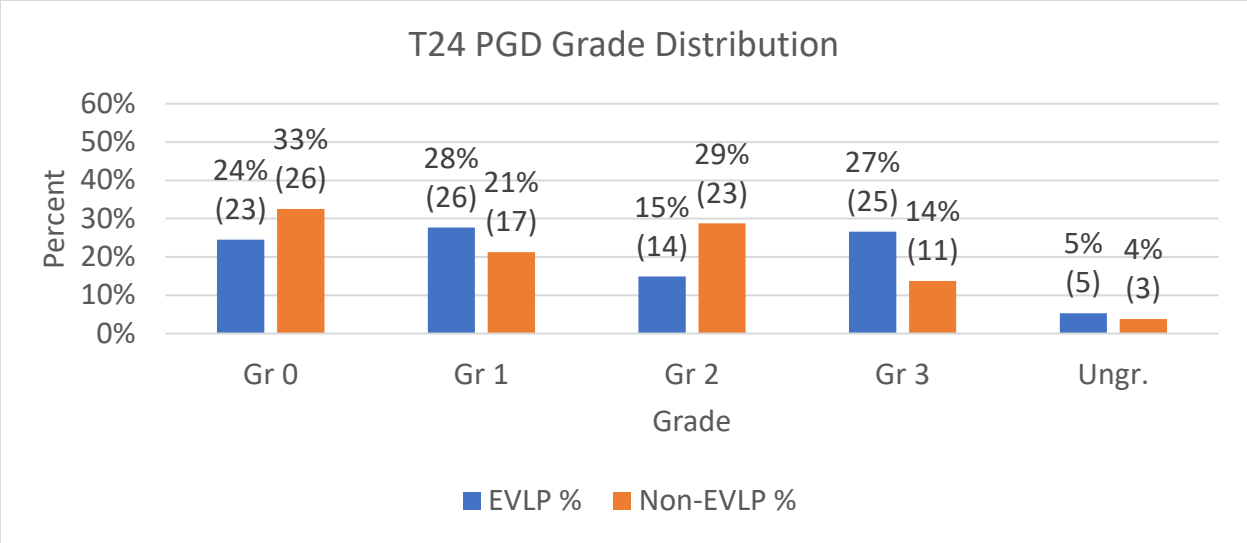
Note: Related was determined as related or possibly related by the CEC.

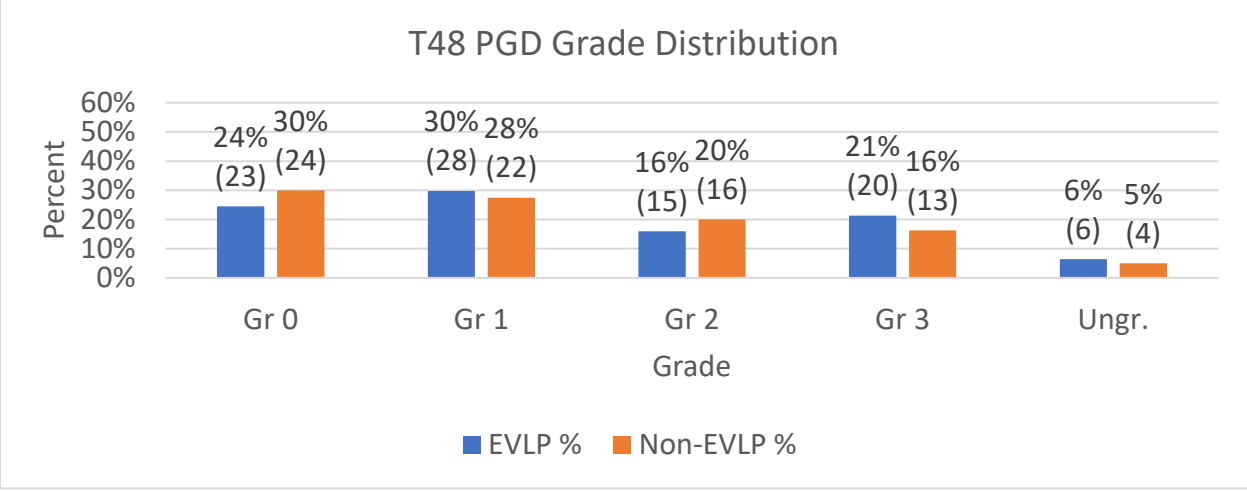
Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per group.

2.3 Primary Graft Dysfunction

Figure 17 presents the distribution of investigator-scored PGD at all time points (0, 24, 48, and 72 hours) for EVLP and non-EVLP subjects in the APS.


T0 PGD Grade Distribution
Percent
60%
50%
40%
30%
20%
10%
0%
21% (20)
41% (33)
13% (12)
15% (12)
11% (10)
15% (12)
47% (44)
24% (19)
7% (7)
4% (3)
Gr 0
Gr 1
Gr 2
Gr 3
Ungr.
Grade
EVLP %
Non-EVLP %


T24 PGD Grade Distribution
Percent
60%
50%
40%
30%
20%
10%
0%
24% (23)
33% (26)
28% (26)
21% (17)
15% (14)
29% (23)
27% (25)
14% (11)
5% (5)
4% (3)
Gr 0
Gr 1
Gr 2
Gr 3
Ungr.
Grade
EVLP %
Non-EVLP %


T48 PGD Grade Distribution
Percent
60%
50%
40%
30%
20%
10%
0%
24% (23)
30% (24)
30% (28)
28% (22)
16% (15)
20% (16)
21% (20)
16% (13)
6% (6)
5% (4)
Gr 0
Gr 1
Gr 2
Gr 3
Ungr.
Grade
EVLP %
Non-EVLP %

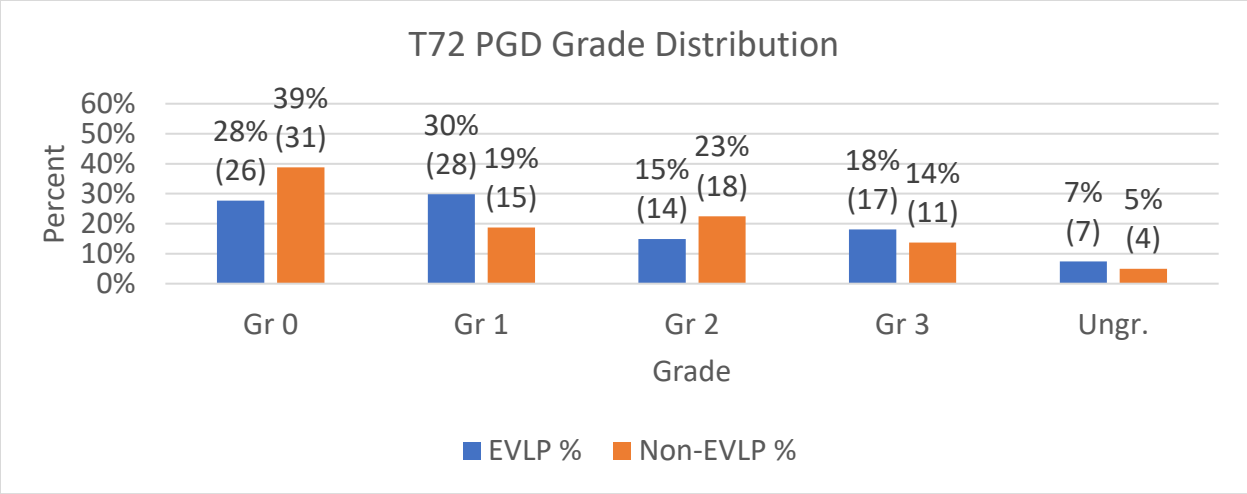
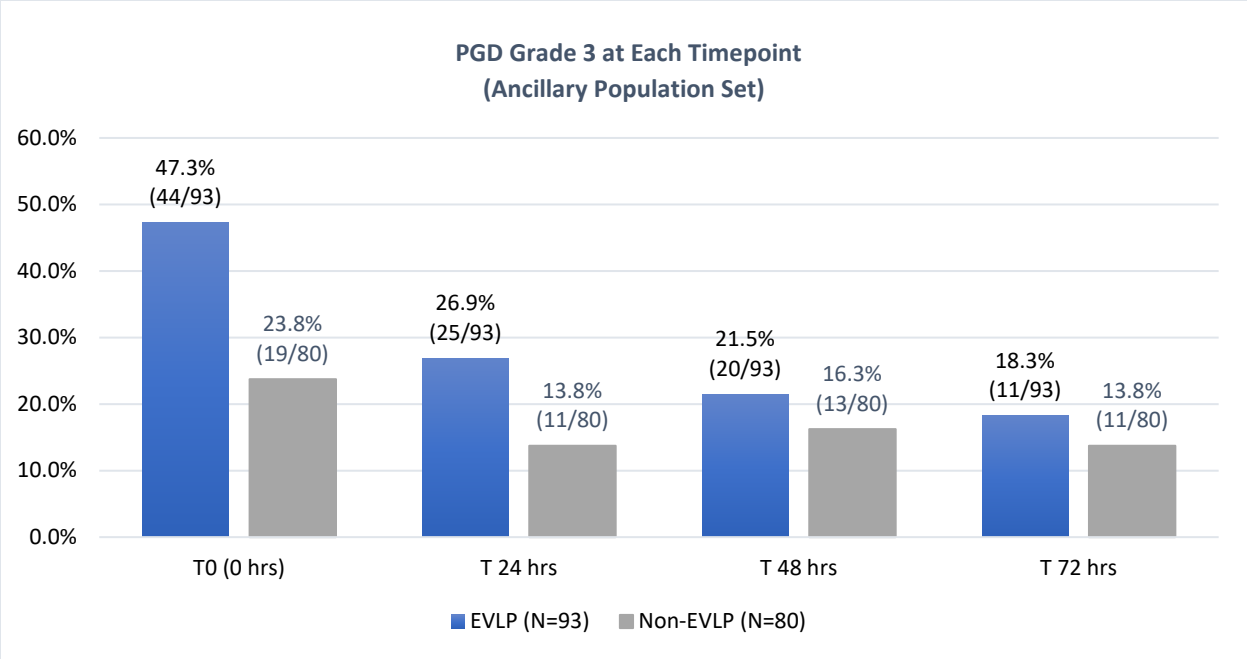
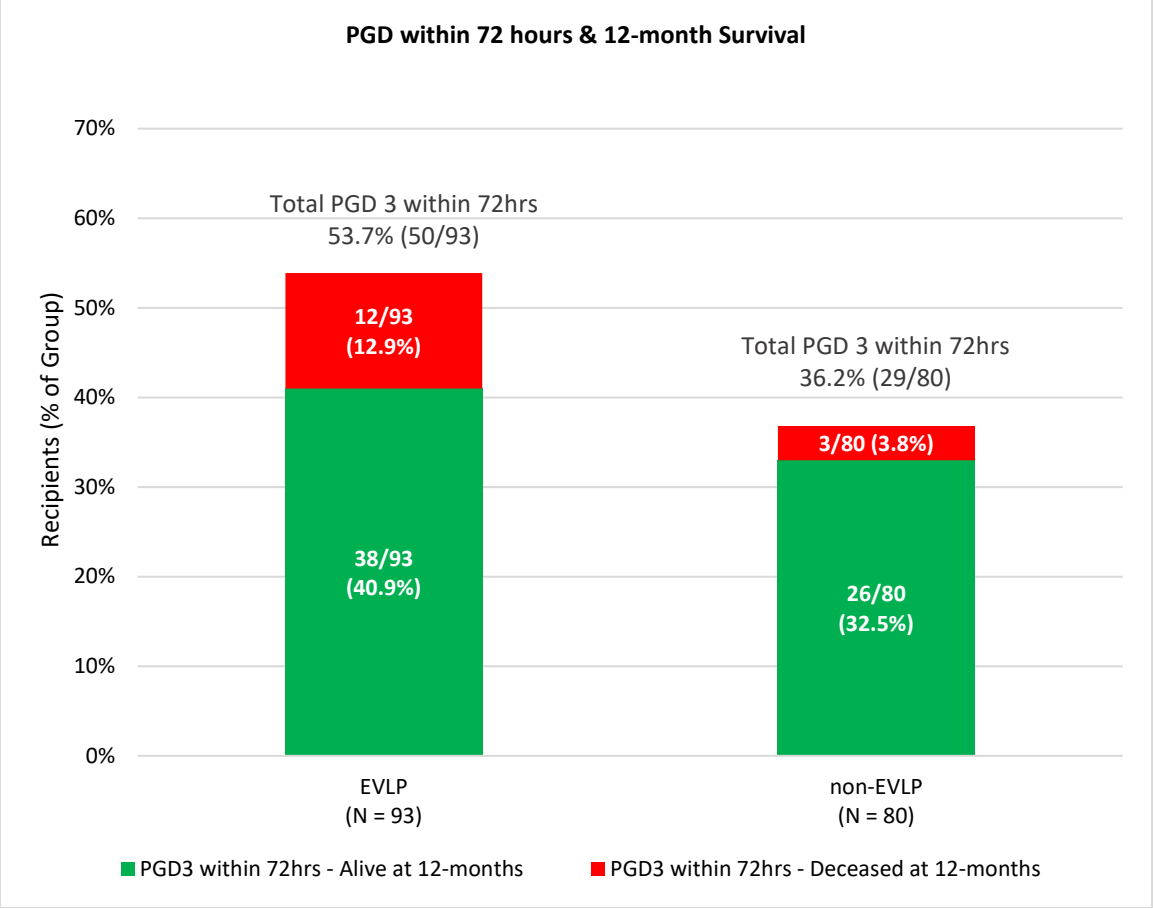


Figure 17: Distribution of Investigator-Scored PGD at All Time Points - Ancillary Population Set

Figure 18 presents the distribution of PGD 3. 53% of EVLP subjects developed PGD 3, compared to 36% of non-EVLP subjects, a rate of PGD 3 within 72 hours proportionately 47% higher than that observed in non-EVLP subjects. The prevalence of PGD 3 in both groups decreased over time, such that at 72 hours the proportions of subjects with PGD 3 were similar (18% EVLP, 14% non-EVLP).

Of the 15 EVLP subjects who died by one year, 12 (80%) had experienced PGD 3 within 72 hours; those 12 subjects represented 24% of the 50 EVLP subjects with PGD 3 Note: one subject in the EVLP Group died during the transplant procedure and therefore was not assessed for PGD at any timepoint). Of the 6 non-EVLP subjects who died by one year, 6 (50%) had experienced PGD 3 within 72 hours; those 3 subjects represented 10% of the 25 non-EVLP subjects with PGD 3. PGD 3 thus both occurred more frequently in EVLP subjects than non-EVLP subjects and appeared more correlated with 12-month mortality (see Figure 18).


PGD Grade 3 at Each Timepoint
(Ancillary Population Set)
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
47.3% (44/93)
23.8% (19/80)
26.9% (25/93)
13.8% (11/80)
21.5% (20/93)
16.3% (13/80)
18.3% (11/93)
13.8% (11/80)
T0 (0 hrs)
T 24 hrs
T 48 hrs
T 72 hrs
EVLP (N=93)
Non-EVLP (N=80)


PGD within 72 hours & 12-month Survival
70%
60%
50%
40%
30%
20%
10%
0%
Recipients (% of Group)
Total PGD 3 within 72hrs
53.7% (50/93)
12/93 (12.9%)
38/93 (40.9%)
Total PGD 3 within 72hrs
36.2% (29/80)
3/80 (3.8%)
26/80 (32.5%)
EVLP (N = 93)
non-EVLP (N = 80)
PGD3 within 72hrs - Alive at 12-months
PGD3 within 72hrs - Deceased at 12-months

PGD 3 within 72 hours	Yes	Yes	No	No	N/A*
12-month status	Alive	Dead	Alive	Dead	Dead
EVLP					
SLT	14	3	6	1	1
DLT	24	9	35	1	0
Total	38	12	41	2	1
Non-EVLP					
SLT	9	0	14	0	0
DLT	17	3	34	3	0
Total	26	3	48	3	0
TOTAL	64	15	89	5	1

*Patient died during the transplant procedure. No PGD scoring was completed.

Figure 18: Distribution of PGD 3 at All Time Points - Ancillary Population Set

Table 22: Correlation of PGD 3 and 12-Month Survival- Ancillary Population Set

PGD 3 within 72 hours	EVLP N=93		Non-EVLP N = 80	
	Alive	Dead	Alive	Dead
No PGD 3	41	2	48	3
DLT	38	12	26	3
Phi Coefficient (φ)	0.270		0.081	
PGD 3 at 72 hours				
No PGD 3	67	9	64	5
DLT	12	5	10	1
Phi Coefficient (φ)	0.190		0.024	

A phi coefficient value > 0.100 and <0.300 indicates a weak correlation

2.4 Ventilator Support and Post-Operative ECMO

Ventilator Support

Compared to non-EVLP subjects, the duration of post-operative ventilatory support (mean and median) was substantially longer for EVLP subjects, both in APS (Table 23) and in MAS populations (Table 24).

Table 23: Summary of Duration on Ventilator Support – Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
Duration on Ventilator Support[a] (Hours)						
Mean	518.48	386.09	421.30	153.35	269.70	236.25
SD	1224.124	543.376	778.492	281.404	610.170	537.337
Median	37.03	135.60	95.28	43.28	48.02	43.77
Min - Max	2.6 – 4562.0	9.1 – 2643.7	2.6 – 4562.0	6.9 – 1123.9	9.4 – 4174.9	6.9 – 4174.9

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Duration of ventilator support was measured as the total number of hours post-transplant where ventilator support was required prior to the initial hospital discharge.

Table 24: Summary of Duration on Ventilator Support - Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Duration on Ventilator Support[a] (Hours)						
Mean	394.76	426.34	417.55	155.65	269.70	237.94
SD	1043.260	580.903	731.780	287.805	610.170	540.597
Median	36.26	176.70	89.60	41.77	48.02	43.75
Min - Max	2.6 - 4562.0	9.1 - 2643.7	2.6 - 4562.0	6.9 - 1123.9	9.4 - 4174.9	6.9 - 4174.9

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant
a Duration of ventilator support was measured as the total number of hours post-transplant where ventilator support was required prior to the initial hospital discharge.

Post-operative ECMO

Similarly, the use of ECMO post-operatively was more common for EVLP recipients (Table 25 (APS) and Table 26 (MAS). In APS, 20% of EVLP subjects and 11% of non-EVLP subjects were managed with ECMO after the transplantation.

Table 25: Summary of ECMO Post-transplant – Ancillary Population

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
ECMO Post-transplant Prior to Initial Discharge, n (%)						
Yes	5 (20.0)	14 (20.3)	19 (20.2)	3 (13.0)	6 (10.5)	9 (11.3)
No	20 (80.0)	55 (79.7)	75 (79.8)	20 (87.0)	51 (89.5)	71 (88.8)

Abbreviations: DLT, double lung transplant; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; SLT, single lung transplant
Note: Percentages were based on the total number (N) of subjects in the Matched Analysis Set per group.

Of the 19 EVLP ECMO patients, 14 (74%) involved donor lungs whose EVLP observation time periods were greater than the cohort's median duration of 3.79 hours; conversely 75 EVLP patients did not receive ECMO, and the majority of them (42 (56%)) had donor lungs with EVLP observation times shorter than the median. Similar associations regarding the need for post-operative ECMO in EVLP subjects were seen with the parameters of TPT (> median time, n=18) and donor criteria type (extended criteria, n=19).

Only 1 EVLP and 1 non-EVLP subject had been on ECMO pre-operatively and then required ECMO post-operatively.

ECMO use patterns and correlations were similar in the MAS population.

Table 26: Summary of ECMO Post-transplant - Matched Analysis Set

	EVLP			Non-EVLP		
	SLT (N=22)	**DLT (N=57)**	**Overall (N=79)**	**SLT (N=22)**	**DLT (N=57)**	**Overall (N=79)**
ECMO Post-transplant Prior to Initial Discharge, n (%)						
Yes	4 (18.2)	12 (21.1)	16 (20.3)	3 (13.6)	6 (10.5)	9 (11.4)
No	18 (81.8)	45 (78.9)	63 (79.7)	19 (86.4)	51 (89.5)	70 (88.6)

Abbreviations: DLT, double lung transplant; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; SLT, single lung transplant

Note: Percentages were based on the total number (N) of subjects in the Matched Analysis Set per group.

2.5 ICU Length of Stay

ICU length of stay and initial hospitalization length of stay were generally clinically similar for the two groups.

For MAS, in the EVLP group, overall median ICU LOS was 11.5 days (range: 3 to 121) with subjects in the DLT subgroup having a lengthier stay (13 days) than the SLT subgroup (5 days). In the non-EVLP group, overall median ICU LOS was 10 days (range: 2 to 169) with subjects in the DLT subgroup also having a lengthier stay (10 days) than the SLT subgroup (6.5 days).

Table 27: Summary of ICU Length of Stay - Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	**DLT (N=57)**	**Overall (N=79)**	**SLT (N=22)**	**DLT (N=57)**	**Overall (N=79)**
ICU Length of Stay[a] (Days)						
Mean	19.19	20.51	20.15	12.95	17.23	16.04
SD	30.180	21.058	23.652	13.947	24.330	21.934
Median	5.00	13.00	11.50	6.50	10.00	10.00
Min - Max	3.0 - 121.0	3.0 - 93.0	3.0 - 121.0	3.0 - 60.0	2.0 - 169.0	2.0 - 169.0
n	21	57	78	22	57	79

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; ICU, intensive care unit; SLT, single lung transplant

a ICU length of stay was measured as the total number of days post-transplant in the ICU until initial hospital discharge, inclusive of ICU readmissions during that hospitalization.

Note: n represents the number of subjects contributing to summary statistics.

2.6 Hospital Length of Stay

For MAS, in the EVLP group, overall median hospital LOS was 27.0 days (range: 2 to 227), with subjects in the DLT subgroup having a lengthier stay (31 days) than the SLT subgroup (19.5 days). In the non-EVLP group, overall median hospital LOS was 29.0 days (range: 8 to 229), with subjects in the DLT subgroup also having a lengthier stay (30 days) than the SLT subgroup (17 days).

Table 28 Summary of Hospital Length of Stay - Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Hospitalization Length of Stay[a] (Days)						
Mean	37.68	44.39	42.52	27.14	44.23	39.47
SD	51.677	34.185	39.587	25.255	42.587	39.157
Median	19.50	31.00	27.00	17.00	30.00	29.00
Min - Max	2.0 - 227.0	8.0 - 146.0	2.0 - 227.0	8.0 - 93.0	10.0 - 229.0	8.0 - 229.0

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant
a Hospital length of stay was measured as the total number of days in the hospital prior to initial discharge post-transplant.

ICU and hospital lengths of stay showed similar patterns for APS.

2.7 Chronic Lung Allograft Dysfunction

Rates of CLAD were low in both EVLP and non-EVLP recipients. This finding is unsurprising, given the limited follow-up duration of only one year.

CLAD rate showed a similar pattern for the APS.

Table 29: Summary of Rate of CLAD During 12-Months Post-Transplant – Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Rate of Diagnosis of CLAD[a], n (%)						
Yes	1 (4.5)	1 (1.8)	2 (2.5)	1 (4.5)	0 (0.0)	1 (1.3)
No	20 (90.9)	53 (93.0)	73 (92.4)	21 (95.5)	56 (98.2)	77 (97.5)
Missing	1 (4.5)	3 (5.3)	4 (5.1)	0 (0.0)	1 (1.8)	1 (1.3)

Abbreviations: CLAD, chronic lung allograft dysfunction; DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant
a Rate of diagnosis of CLAD was any occurrence of CLAD throughout the duration of the study.
Note: Percentages were based on the total number (N) of subjects in the Matched Analysis Set per group.

2.8 Respiratory Failure

For MAS, in the EVLP group overall, 24/79 (30.4%) subjects developed respiratory failure post-transplant (5 SLT and 19 DLT). In the non-EVLP group overall, 18/79 (22.8%) subjects developed respiratory failure post-transplant (4 SLT and 14 DLT). Respiratory failure showed a similar pattern for APS.

Table 30: Summary of Rate of Respiratory Failure - Matched Analysis Set

Category	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
Rate of Respiratory Failure[a], n (%)						
Yes	5 (22.7)	19 (33.3)	24 (30.4)	4 (18.2)	14 (24.6)	18 (22.8)
No	17 (77.3)	38 (66.7)	55 (69.6)	18 (81.8)	43 (75.4)	61 (77.2)
95 % CI[b]	(7.8, 45.4)	(21.4, 47.1)	(20.5, 41.8)	(5.2, 40.3)	(14.1, 37.8)	(14.1, 33.6)

Abbreviations: AE, adverse event; CI, confidence interval; DLT, double lung transplant; EVLP, ex vivo lung perfusion; SLT, single lung transplant

a Rate of respiratory failure was recorded as any respiratory failure throughout the duration of the study as recorded on the AE eCRF.

b Exact binomial was used to construct CI. The 95% CI was constructed around the proportion of subjects with respiratory failure throughout the study.

Note: Percentages were based on the total number (N) of subjects in the Matched Analysis Set per group.

2.9 Forced Expiratory Volume in 1 Second (FEV_1)

At all time points, mean and median recorded FEV_1 were modestly higher in the non-EVLP group among the Matched Analysis Set. Data capture, however, was not complete for pulmonary function testing. FEV_1 showed a similar pattern for APS.

Table 31: Summary of FEV1 - Matched Analysis Set

Timepoint	EVLP			Non-EVLP		
	SLT (N=22)	DLT (N=57)	Overall (N=79)	SLT (N=22)	DLT (N=57)	Overall (N=79)
FEV1 Day 90 Post-transplant						
Mean	67.0	66.5	66.6	73.7	76.2	75.5
SD	18.20	21.04	20.03	19.39	20.39	19.98
Median	69.0	65.0	67.0	69.0	74.0	73.0
Min - Max	28 - 102	13 - 116	13 - 116	46 - 122	30 - 117	30 - 122
n	19	41	60	18	45	63
FEV1 Month 6 Post-transplant						
Mean	67.9	69.6	69.1	72.9	82.1	79.4
SD	18.18	18.26	18.10	19.11	20.79	20.60
Median	67.0	71.0	68.0	73.0	80.0	79.0
Min - Max	41 - 106	28 - 128	28 - 128	36 - 125	34 - 123	34 - 125
n	18	43	61	19	46	65
FEV1 Month 12 Post-transplant						
Mean	72.5	74.8	74.1	73.9	85.2	82.0
SD	19.67	17.81	18.25	25.20	25.86	26.01
Median	74.0	76.0	74.0	75.5	85.0	79.5
Min - Max	23 - 110	45 - 129	23 - 129	37 - 128	23 - 156	23 - 156
n	19	45	64	20	50	70

Abbreviations: DLT, double lung transplant; EVLP, ex vivo lung perfusion; FEV_1, forced expiratory volume in 1 second; SLT, single lung transplant

Note: n represents the number of subjects contributing to summary statistics.

Adverse Effects that Occurred in the PMA Clinical Study:

Consistent with the complex clinical presentations of lung transplant recipients, both the EVLP and non-EVLP groups demonstrated similarly high occurrences of AEs. Intervention-emergent AEs were defined as those events newly occurring or worsening from Baseline (Day 0): 85 out of 94 EVLP subjects (90.4%) and 73 out of 80 non-EVLP subjects (91.3%) experienced at least 1 intervention-emergent AE during the study (Table 32).

The most frequently reported adverse events (>3%) by System Organ Class (SOC) in both groups were "Respiratory, thoracic, and mediastinal disorders," followed by "Infections and infestations," and "Immune system disorders." A higher proportion of subjects in the EVLP group, 60 out of 94 (63.8%), experienced AEs assessed by Investigators as severe, compared to 38 out of 80 (47.5%) subjects in the non-EVLP group. Intervention-emergent serious AEs (SAEs) with "respiratory, thoracic, and mediastinal disorders" were the predominant SOC observed in both groups, but the incidence was substantially higher in EVLP (61.7% EVLP subjects, 43.8% non-EVLP subjects (APS)). Notably, the EVLP group had higher incidences of the respiratory-related SAEs respiratory failure, pulmonary embolism, and bronchostenosis. The EVLP group had lower incidence of immune system disorders SAEs; this category included allograft rejection.

Assessments by the Investigators and CEC indicated that many of the intervention-emergent AEs were related to the lung transplant in both groups, with a slightly higher assessment rate by Investigators in the EVLP group.

Table 32: Investigator-Reported Intervention-Emergent Adverse Events by SOC (>3%) - Ancillary Population Set

System Organ Class	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
All body systems, n (%)	21 (84.0)	64 (92.8)	85 (90.4)	22 (95.7)	51 (89.5)	73 (91.3)
Blood and lymphatic system disorders, n (%)	2 (8.0)	1 (1.4)	3 (3.2)	2 (8.7)	7 (12.3)	9 (11.3)
Cardiac disorders, n (%)	7 (28.0)	13 (18.8)	20 (21.3)	5 (21.7)	9 (15.8)	14 (17.5)
Eye disorders, n (%)	1 (4.0)	1 (1.4)	2 (2.1)	1 (4.3)	1 (1.8)	2 (2.5)
Gastrointestinal disorders, n (%)	6 (24.0)	19 (27.5)	25 (26.6)	4 (17.4)	11 (19.3)	15 (18.8)
General disorders and administration site conditions, n (%)	2 (8.0)	5 (7.2)	7 (7.4)	0 (0.0)	2 (3.5)	2 (2.5)
Hepatobiliary disorders, n (%)	0 (0.0)	4 (5.8)	4 (4.3)	1 (4.3)	7 (12.3)	8 (10.0)
Immune system disorders, n (%)	9 (36.0)	25 (36.2)	34 (36.2)	12 (52.2)	21 (36.8)	33 (41.3)
Infections and infestations, n (%)	14 (56.0)	39 (56.5)	53 (56.4)	10 (43.5)	31 (54.4)	41 (51.3)
Injury, poisoning and procedural complications, n (%)	3 (12.0)	18 (26.1)	21 (22.3)	4 (17.4)	15 (26.3)	19 (23.8)
Investigations, n (%)	5 (20.0)	12 (17.4)	17 (18.1)	6 (26.1)	12 (21.1)	18 (22.5)
Metabolism and nutrition disorders, n (%)	5 (20.0)	12 (17.4)	17 (18.1)	6 (26.1)	13 (22.8)	19 (23.8)
Musculoskeletal and connective tissue disorders, n (%)	0 (0.0)	2 (2.9)	2 (2.1)	1 (4.3)	0 (0.0)	1 (1.3)

System Organ Class	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	2 (3.5)	3 (3.8)
Nervous system disorders, n (%)	1 (4.0)	11 (15.9)	12 (12.8)	4 (17.4)	8 (14.0)	12 (15.0)
Product issues, n (%)	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	0 (0.0)	1 (1.3)
Psychiatric disorders, n (%)	1 (4.0)	1 (1.4)	2 (2.1)	1 (4.3)	3 (5.3)	4 (5.0)
Renal and urinary disorders, n (%)	3 (12.0)	11 (15.9)	14 (14.9)	2 (8.7)	5 (8.8)	7 (8.8)
Respiratory, thoracic and mediastinal disorders, n (%)	16 (64.0)	49 (71.0)	65 (69.1)	11 (47.8)	38 (66.7)	49 (61.3)
Skin and subcutaneous tissue disorders, n (%)	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	2 (3.5)	3 (3.8)
Vascular disorders, n (%)	3 (12.0)	4 (5.8)	7 (7.4)	1 (4.3)	6 (10.5)	7 (8.8)

Abbreviations: AE, adverse event; DLT, double lung transplant; EVLP, ex vivo lung perfusion; MedDRA, Medical Dictionary for Regulatory Activities; SLT, single lung transplant; SOC, System Organ Class
Note: Intervention-emergent AEs were defined as AEs that were newly occurring or worsening from Baseline (Day 0).
Note: Subjects with multiple events within each SOC were counted only once for that SOC.
Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per transplant group.
MedDRA Version 26.0 was used for AE coding.

Table 33: Investigator- Reported Intervention-Emergent Serious Adverse Events by SOC (>3%) - Ancillary Population Set

System Organ Class	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
All body systems, n (%)	20 (80.0)	57 (82.6)	77 (81.9)	20 (87.0)	43 (75.4)	63 (78.8)
Blood and lymphatic system disorders, n (%)	2 (8.0)	1 (1.4)	3 (3.2)	2 (8.7)	6 (10.5)	8 (10.0)
Cardiac disorders, n (%)	7 (28.0)	9 (13.0)	16 (17.0)	3 (13.0)	3 (5.3)	6 (7.5)
Eye disorders, n (%)	1 (4.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.8)	1 (1.3)
Gastrointestinal disorders, n (%)	3 (12.0)	10 (14.5)	13 (13.8)	2 (8.7)	7 (12.3)	9 (11.3)
General disorders and administration site conditions, n (%)	2 (8.0)	3 (4.3)	5 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders, n (%)	3 (12.0)	12 (17.4)	15 (16.0)	9 (39.1)	13 (22.8)	22 (27.5)
Infections and infestations, n (%)	12 (48.0)	29 (42.0)	41 (43.6)	8 (34.8)	23 (40.4)	31 (38.8)
Injury, poisoning and procedural complications, n (%)	2 (8.0)	14 (20.3)	16 (17.0)	4 (17.4)	14 (24.6)	18 (22.5)
Investigations, n (%)	4 (16.0)	5 (7.2)	9 (9.6)	1 (4.3)	4 (7.0)	5 (6.3)
Metabolism and nutrition disorders, n (%)	1 (4.0)	3 (4.3)	4 (4.3)	2 (8.7)	4 (7.0)	6 (7.5)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	2 (3.5)	3 (3.8)
Nervous system disorders, n (%)	1 (4.0)	6 (8.7)	7 (7.4)	1 (4.3)	6 (10.5)	7 (8.8)
Product issues, n (%)	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	0 (0.0)	1 (1.3)
Psychiatric disorders	1 (4.0)	0 (0.0)	1 (1.1)	0 (0.0)	2 (3.5)	2 (2.5)
Renal and urinary disorders, n (%)	2 (8.0)	6 (8.7)	8 (8.5)	0 (0.0)	3 (5.3)	3 (3.8)
Respiratory, thoracic and mediastinal disorders, n (%)	14 (56.0)	44 (63.8)	58 (61.7)	9 (39.1)	26 (45.6)	35 (43.8)
Vascular disorders, n (%)	1 (4.0)	3 (4.3)	4 (4.3)	1 (4.3)	3 (5.3)	4 (5.0)

Abbreviations: AE, adverse event, DLT, double lung transplant; EVLP, ex vivo lung perfusion; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLT, single lung transplant; SOC, System Organ Class

Note: Intervention-emergent SAEs were defined as SAEs that were newly occurring or worsening from Baseline (Day 0).
Note: Subjects with multiple events within each SOC were counted only once for that SOC.
Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per transplant group.
Note: MedDRA Version 26.0 was used for AE coding.

Table 34: Overview of All Investigator-Reported and CEC-Adjudicated Intervention-Emergent Serious Adverse Events Related to Lung Transplant, EVLP, and ECMO – Ancillary Population Set

Category	EVLP			Non-EVLP		
	SLT (N=25)	DLT (N=69)	Overall (N=94)	SLT (N=23)	DLT (N=57)	Overall (N=80)
Relationship to Lung Transplant by Investigator, n (%)						
Related	15 (60.0)	48 (69.6)	63 (67.0)	11 (47.8)	33 (57.9)	44 (55.0)
Possibly Related	5 (20.0)	2 (2.9)	7 (7.4)	4 (17.4)	7 (12.3)	11 (13.8)
Unlikely Related	0 (0.0)	1 (1.4)	1 (1.1)	2 (8.7)	2 (3.5)	4 (5.0)
Not Related	0 (0.0)	6 (8.7%)	6 (6.4)	3 (13.0)	1 (1.8)	4 (5.0)
Relationship to Lung Transplant by CEC, n (%)						
Related	13 (52.0)	45 (65.2)	58 (61.7)	14 (60.9)	35 (61.4)	49 (61.3)
Possibly Related	5 (20.0)	5 (7.2)	10 (10.6)	3 (13.0)	7 (12.3)	10 (12.5)
Unlikely Related	0 (0.0)	5 (7.2)	5 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)
Not Related	0 (0.0)	1 (1.4)	1 (1.1)	2 (8.7)	1 (1.8)	3 (3.8)
Relationship to Device/EVLP by Investigator, n (%)						
Related	0 (0.0)	0 (0.0)	0 (0.0)			
Possibly Related	3 (12.0)	13 (18.8)	16 (17.0)			
Unlikely Related	11 (44.0)	26 (37.7)	37 (39.4)			
Not Related	6 (24.0)	18 (26.1)	24 (25.5)			
Relationship to Device/EVLP by CEC, n (%)						
Related	0 (0.0)	0 (0.0)	0 (0.0)			
Possibly Related	7 (28.0)	23 (33.3)	30 (31.9)			
Unlikely Related	5 (20.0)	19 (27.5)	24 (25.5)			
Not Related	6 (24.0)	14 (20.3)	20 (21.3)			
Relationship to ECMO by Investigator, n (%)						
Related	0 (0.0)	3 (4.3)	3 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)
Possibly Related	1 (4.0)	1 (1.4)	2 (2.1)	0 (0.0)	3 (5.3)	3 (3.8)
Unlikely Related	1 (4.0)	2 (2.9)	3 (3.2)	1 (4.3)	1 (1.8)	2 (2.5)
Not Related	1 (4.0)	7 (10.1)	8 (8.5)	1 (4.3)	1 (1.8)	2 (2.5)
Not Applicable	17 (68.0)	44 (63.8)	61 (64.9)	18 (78.3)	38 (66.7)	56 (70.0)
Relationship to ECMO by CEC, n (%)						
Related	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Possibly Related	2 (8.0)	5 (7.2)	7 (7.4)	0 (0.0)	2 (3.5)	2 (2.5)
Unlikely Related	1 (4.0)	5 (7.2)	6 (6.4)	0 (0.0)	1 (1.8)	1 (1.3)
Not Related	0 (0.0)	1 (1.4)	1 (1.1)	1 (4.3)	0 (0.0)	1 (1.3)
Not Applicable	15 (60.0)	45 (65.2)	60 (63.8)	18 (78.3)	40 (70.2)	58 (72.5)

Abbreviations: CEC, Clinical Events Committee; DLT, double lung transplant; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; SAE, serious adverse event; SLT, single lung transplant
Note: Intervention-emergent SAEs were defined as SAEs that were newly occurring or worsening from Baseline (Day 0).
Note: Percentages were based on the total number (N) of subjects in the Ancillary Population Set per transplant group.

Utilization Rate of EVLP Lungs

Over the course of enrollment, the Sponsor received 326 calls to screen donor lungs for inclusion in the study ("referrals"). These referrals came from transplant

centers or OPOs for reasons delineated above. Of these referrals 131 (40.2%) underwent LungFX assessment. Of the 131 EVLP assessments 91 (69.5%) were accepted for transplantation.

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 235 investigators, including 26 Principal Investigators, with the remainder serving as Sub-Investigators. Of these 2[a] full-time or part-time employees of the sponsor and 1[a] had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 0
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1[a]

[a] Site 100 was a Sponsor-controlled facility. All personnel of Site 100 were employees or contractors of the Sponsor.

As stated, there were 2[a] Investigators under Site 100 that were employed by the Sponsor; however, this relationship did not compromise the integrity of the data. One of the 2 sites, Site 100 Investigators, Dr. Jordan Shin, did hold significant equity in the Sponsor company, which necessitated the submission of FDA Form 3455. The Sponsor has completed and submitted FDA Form 3455, accompanied by a brief explanatory statement of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests, which is included in the submission. In summary, the applicant has adequately disclosed the financial interest/arrangements with Investigators.

F. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel, an FDA advisory committee, for review and recommendation

because the information in the PMA substantially duplicates information previously reviewed by this panel.

G. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

a. Safety and Effectiveness Conclusions

There have been two U.S. IDE trials of the LungFX device. A feasibility study (G140021) enrolled subjects between 2015 and 2018, and it demonstrated 12-month survival of 89% after transplantation of EVLP donor lungs; at 5 years, survival was 50%. These results were clinically similar to the survival observed in the feasibility study's control arm cohort (Table 3). The feasibility experience informed the design of the CLES Pivotal Study (G170312). The CLES Pivotal Study constitutes the primary data set supporting this PMA. This trial was a prospective, controlled, non-randomized study of 94 treatment-arm subjects who were transplanted with donor lungs after EVLP assessment at a centralized facility. The donor lungs referred for EVLP evaluation had to have been designated by the responsible OPO as otherwise not able to be used for any transplantation in the U.S., and the PMA sponsor could either accept or reject a referral. The study included conventionally described "standard" and "extended" criteria donor organs; lungs procured from DBD and DCD donors; and single- and double-lung grafts. The control arm consisted of contemporaneous, loosely matched recipients of donor lungs accepted and transplanted without the need for re-assessment after procurement.

The primary endpoint evaluated twelve-month survival within the EVLP group. A Bayesian statistical comparison (95% posterior probability) to the twelve-month survival performance goal of 81.2% was pre-specified. Comparisons to the control arm's results were also made, but the study was not randomized, as the premise of LungFX is that its EVLP only be used under the condition that donor lungs cannot be placed with a recipient unless the clinician has the opportunity with EVLP to re-consider the initial no-transplant decision.

The primary endpoint, 12-month survival, was 84% (95% CI: 75.0, 90.8). The primary endpoint result did not meet the pre-specified performance goal for survival after transplantation of EVLP lungs.

Comparison of EVLP's primary endpoint metric to the non-EVLP control cohorts demonstrated lower point estimates of 12-month survival after EVLP. Compared to non-EVLP recipients, EVLP recipients experienced proportionately more lung graft-related mortality (11% versus 6%).

Longer-term (Kaplan-Meier) survival estimates demonstrated a survival advantage for non-EVLP transplant recipients as compared to LungFX EVLP transplant recipients at 2 and 3 years. The differences were most notable in several pre-specified sub-group analyses, including extended criteria donors and single lung transplants. Survival among DBD donors was generally similar between EVLP and non-EVLP, but survival for EVLP DCD donor lung recipients was lower than that observed both in DCD donors in the contemporaneous SRTR/OPTN database and in DBD donors in the pivotal study (few non-EVLP subjects were DCD).

LungFX inherently leads to long preservation times, as it entails two separate periods of preservation with cold static solution in addition to a period of warm perfusion EVLP having a minimum duration of 3 hours. The CLES Pivotal Study clearly demonstrated that LungFX increases the cumulative time from organ procurement to transplantation as compared to non-EVLP preservation. Prolongation of donor organ preservation was quantified by comparing TPT between groups in the Ancillary Population Set. LungFX allowed for markedly longer total preservation times (between approximately 8-20 hours) as compared to non-EVLP preservation. However, stratified survival estimates did suggest reduced recipient survival rate in the setting of longer (> 13 hours) total preservation times. A further analysis of EVLP subjects alone demonstrated lower survival in the setting of longer (> ~4 hours) 2nd cold-ischemic times (CIT-2), though these analyses did not account for multiplicity.

LungFX EVLP did increase the use of deceased donor lungs for transplant. Of the 131 organs deemed by the source OPO not otherwise usable and then sent for EVLP, 91 (69.5%) were able to be successfully placed and transplanted into 94 study subjects. The option for LungFX was specifically intended not to circumvent the standard match-run algorithm of OPTN organ allocation. Nonetheless, “allocation ended” (e.g., match list exhausted) was an infrequent reason (10%) for EVLP referral in the CLES Pivotal Study; the most frequent reasons for using LungFX were DCD donor (28%), intra-operative decline of provisionally accepted donor lungs (27%), and OPO/transplant center “logistical challenges” (26%). Of note, there were 60 cases where an initial referral was made to the Sponsor for EVLP that were subsequently allocated for standard-of-care transplantation after further review by a transplant center. This volume of re-considered EVLP is equivalent to 64% of the number of cases that did proceed to EVLP. Although such instances of changing a procurement plan are not inherently deleterious, they may suggest that the general process for identifying lungs “that would not otherwise be used” is not optimized; optimal referral/acceptance criteria for LungFX is essential, given the observed survival results for EVLP and non-EVLP lungs in the CLES Pivotal Study.

b. Safety Conclusions and Adverse Events

PGD 3 occurred more frequently in EVLP subjects. LungFX was associated with a higher incidence of PGD 3 within 72 hours (53% of subjects) than the incidence in non-EVLP subjects (36%). Twenty-four percent of EVLP subjects who developed PGD 3 died within 1 year; ten percent of non-EVLP subjects who had PGD 3 died by one year.

The proportion of subjects requiring post-transplantation ECMO was approximately twice as high in the EVLP group compared to non-EVLP. Duration of mechanical ventilatory support was also higher among the EVLP group. However, ICU and hospital lengths of stay were clinically similar in both groups.

Rates of CLAD at 12 months were low overall, and graft failure leading to re-transplantation did not occur during the 12-month primary endpoint time-period. However, CLAD is a clinical diagnosis that generally manifests at time periods later than one year.

Both the EVLP and non-EVLP groups demonstrated similar occurrences of AEs overall, with 85/94 (90.4%) subjects in the EVLP group and 73/80 (91.3%) subjects in the non-EVLP group experiencing at least 1 intervention-emergent AE during the study. However, a higher proportion of subjects in the EVLP group, (60/94 [63.8%]), experienced an intervention-emergent AE assessed by Investigators as severe, compared to 38/80 (47.5%) subjects in the non-EVLP group.

The EVLP group had a higher incidence of respiratory-related SAEs when compared to the non-EVLP group. Serious adverse events occurred frequently in the CLES Pivotal Study, and those involving the respiratory system (notably the events of respiratory failure, pulmonary embolism, and bronchostenosis) had a higher incidence in EVLP subjects as compared to non-EVLP subjects. Consistent with this finding was the observation that both SLT and DLT EVLP subjects developed respiratory failure more frequently after transplant than non-EVLP subjects. EVLP subjects generally required more prolonged periods of invasive respiratory support (mechanical ventilation and/or ECMO). However, the incidences of SAEs specifically adjudicated as related or possibly related to the lung transplant were similar (~ 72% of subjects in both EVLP and non-EVLP groups), and adjudicated relatedness to LungFX was lower: 32% of SAEs were adjudicated as “possibly related” to the device, while none was adjudicated as “related.” Other SAEs were those that typically occur following lung transplant surgery.

c. Benefit-Risk Determination

Summary of Probable Benefits

The CLES Pivotal Study demonstrated that use of the device allowed for the procurement and subsequent transplantation of donor lungs that would not otherwise be used for transplant. This benefit is primarily due to the ability of LungFX to provide clinically relevant data about explanted donor lungs so that a transplant physician might better assess lung function and quality, thereby informing decisions about the suitability of the organ for transplantation. The types of donor lungs studied were heterogeneous in their characteristics, and the aggregate results primarily reflect a donor population defined by an OPO's inability to allocate them to suitable recipients given the myriad dynamics---including allocation time windows and multi-organ donation constraints, incomplete donor and organ information available at procurement, and clinical findings at the time of initial evaluations which raise concerns---that affect the success of matching and placing donor lungs. In this context, LungFX does increase the available donor pool. The device's ability to facilitate transplantation from donation-after-circulatory death donors represents a particular probable benefit to the public health, as this source of donor organs, although increasing substantially in recent years, is still under-utilized in part because of concerns about predicting the variable sequelae of obligatory warm ischemia times.

Use of LungFX also led to renewed consideration of provisionally-accepted donor lungs that would have been pre-procurement turn-downs because of findings made during clinicians' open-chest assessments of the donor. Matching to another potential recipient under such circumstances is often not feasible, and therefore OPO referrals for LungFX EVLP in such scenarios can also be viewed as mechanism to expand the donor pool. In the study, "logistical challenges" as a justification for using EVLP often referred to timing concerns at the recipient transplant center, with the intent to use EVLP because of its ability to provide prolonged preservation times. Importantly, longer-term survival seemed less favorable with longer preservation times, and thus the trial results do not support a paradigm of LungFX referral simply as a means of extending preservation time to allow for resolution of logistical issues such operating room availability at the transplant center. However, in scenarios where preservation times with standard preservation techniques would be unavoidably and unacceptably prolonged (e.g., procurement of lungs from distances with long travel times), leveraging the longer preservation and assessment times inherent in the LungFX device may be appropriate if no other recipient can be matched.

Summary of Risks

Like all medical devices, the LungFX device poses risks. Lung transplantation is an invasive therapy intended to provide sustained, beneficial results for patients over the course of years. Detailed clinical follow-up of CLES Pivotal Study subjects is currently limited to 2-3 years, and data out to this time-period demonstrate survival that, while clinically acceptable for many patients with end-stage lung disease, appears to be lower than survival associated with contemporaneous non-EVLP recipients. By design, LungFX is intended to be utilized only for donor lungs that would not be transplanted without the device, but that characterization is inherently subjective, and it was assigned in the study by investigators and OPOs on a case-by-case basis. As a result, the donor lungs that were referred for and then underwent EVLP constituted a heterogenous group, and pre-specified sub-group analyses suggest that post-transplantation survival after EVLP may vary among those sub-groups. Accordingly, there is uncertainty if the aggregate survival data can uniformly inform all patients' and physicians' decisions to proceed with post-EVLP acceptance of LungFX lungs, as opposed to the alternative risk of remaining on the waiting list for another matching donor offer. The counterfactual to utilizing EVLP in certain scenarios can be better appreciated by considering the CLES Pivotal Study survival data in the context of SRTR data for patients on the waiting list in 2024: pre-transplant mortality overall was 16.2 deaths/100 patient-years, and the rate for Composite Allocation Score (CAS) Group D subjects, which formed three-quarters of the pivotal study's population, was 20.0 deaths/100 patient-years. Overall, 67.9% of 2024's waiting-list candidates were transplanted within 90 days of listing; for patients initially listed around the time of study enrollment beginning in 2019, 78.6% were transplanted within 1 year. As shown previously, SRTR database survival rates after transplantation were higher than LungFX survival rates observed in the pivotal study.

Similarly, LungFX was associated with an increased rate of severe primary graft dysfunction, and the presence of PGD 3 was in turn associated with more mortality in EVLP subjects than in non-EVLP subjects. However, it is uncertain to what extent the observed rate of treatment-arm PGD 3 was a consequence of EVLP *per se*, as opposed to likely confounding factors (such as the proportion of DCD donors).

The presence or absence of a relationship between EVLP and CLAD remains unknown at this time, given the length of follow-up to date. It will be better elucidated by planned longer-term follow-up of the pivotal study subjects in a post-approval study.

Although LungFX provides a presumed benefit of longer preservation times that could ameliorate logistical challenges to successful transplant procedures, there is a risk that the cumulative cold ischemic times (CIT-1 and CIT-2) are themselves deleterious. Data from the pivotal trial may suggest an inverse relationship

between longer-term survival and both TPT and cold ischemia times. Because no transplanted EVLP lungs in the CLES Pivotal Study experienced TPT longer than 20.1 hours, clinical use of LungFX is labelled as not intended to exceed 20 hours. However, the optimal balance of TPT and cumulative cold ischemia times with post-transplantation graft function and survival remains uncertain.

In summary, the principal risk to patients is that transplantation with a donor lung re-assessed with LungFX may have clinically less favorable longer-term survival and/or functional status than would have occurred if transplantation had instead been deferred and a non-EVLP donor became available.

Overall Conclusions

1. Patient Perspective

This submission did not include specific information on patient perspectives for this device. However, the acknowledged preference of patients with lung disease who are placed on the transplant waiting list is to receive an acceptable organ. Each patient's definition of acceptable is unique and reflects the patient's weighing the value of accepting a current lung offer with a predicted clinical outcome versus the value and risks of waiting for another future offer for which predicted clinical outcome is currently unknown. Gaining the patient's informed perspective about donor quality is always important, and use of LungFX in the procurement process increases the need for including patient perspective when considering donor options.

In conclusion, given the available information above, the data support for the use of the LungFX device for centralized, *ex vivo* (outside the body) evaluation of deceased-donor lungs (single and double) that cannot be placed for transplantation by an Organ Procurement Organization (OPO) with any of the matched candidates if using direct-to-recipient procurement and preservation procedures. LungFX provides normothermic perfusion and ventilation of procured donor lungs initially stored with cold static preservation solution.

LungFX is intended to allow for re-assessment, in a controlled environment, of procured donor lungs' suitability for transplantation into male and female patients aged 18 years or older with end-stage lung disease awaiting first time (double or single) lung transplantation the probable benefits outweigh the probable risks.

d. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Given the available information above, the probable benefits outweigh the probable risks of using the LungFX device for *ex vivo* evaluation and assessment of

transplantation suitability of deceased-donor lungs that cannot be placed for transplantation by an Organ Procurement Organization (OPO) with any of the matched candidates if using direct-to-recipient procurement and preservation procedures.

H. CDRH DECISION

CDRH issued an approval order on June 22, 2026. The final clinical conditions of approval cited in the approval order are described below.

In addition to the Annual Report requirements, Lung Bioengineering (LBE) must provide the following data in post-approval study (PAS) reports for each PAS listed below.

1. The Long-Term Follow-Up of EVP-DEV-LTX-301 Participants and CLES [Central Lung Evaluation System] for EVLP [Ex Vivo Lung Preservation] Lung Transplant Recipients is an on-going observational, retrospective review of data obtained from the United Network for Organ Sharing (UNOS) for all lung transplant recipients enrolled in the EVP-DEV-LTX-301 piviotal trial for the LungFX device. The purpose of this study is to obtain long-term, post-transplant follow-up data for up to 5 years for all subjects enrolled in the piviotal trial protocol and 10 additional recipients who received donor lungs following CLES assessment under FDA emergency use exemption. Subjects will be followed for 5 years and data will be collected at years 2, 3, 4 and 5. Data collected include survival status, cause of death, oxygen requirement at rest, occurrence of chronic lung allograft dysfunction (CLAD), physical capacity, work status and graft survival. All analysis will be descriptive in nature.

   PAS Progress Reports must be submitted every six months for the first year and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA. The Final PAS Report should be submitted no later than three months after study completion (i.e., last subject's last follow-up date).

2. The LungFX Post-Approval Study (LungFX PAS) is a prospective, multi-center, all-comers study designed to assess the benefits and risks for lung transplantation patients receiving donor lung(s) assessed with the LungFX device. To evaluate real-world use of the device, the study will include all lung transplant recipients which receive a lung which has been assessed using the LungFX device during the 5 years following PMA approval of LungFX; this includes all donor lungs that are either transplanted without ELVP using LungFX or are evaluated using LungFX regardless of whether the lung is accepted for transplant. This study will evaluate long-term (5-year) outcomes of recipients of LungFX lungs to inform clinician’s and patient’s decision making.

   The first 420 consecutive lung transplant patients enrolled in the LungFX PAS who receive lungs assessed using the LungFX device will constitute the primary analysis cohort for the formal statistical evaluation. Outcomes for these PAS participants will

be compared with those of all other single organ lung transplant recipients in the United States during the same time period as the LungFX recipients in the primary analysis set. Data from an estimated 8,400 patients in the concurrent Organ Procurement and Transplantation Network (OPTN) database will serve as the concurrent comparison cohort.

The primary analysis will compare 1-year patient survival free from graft failure requiring re transplantation between PAS participants and the concurrent OPTN cohort using Kaplan-Meier methods, with corresponding 95% confidence intervals. The study is expected to have 90% power to demonstrate non-inferiority using a non-inferiority margin of 10%. PAS participants will be followed for 5 years post-transplant. Adverse events and primary graft dysfunction data not otherwise captured in the OPTN database will be collected retrospectively from transplant center records unless they are reported spontaneously to the Sponsor during the course of the study. EVLP data will be collected from Lung Bioengineering EVLP records and radiographs collected to calculate primary graft dysfunction and will be adjudicated by an independent adjudication committee.

Patients who receive non-EVLP lung transplants and meet the pre-specified PAS matching criteria will be included in a secondary analysis comparing the 420 LungFX patients with a matched control group. Matching will be performed based on four factors: transplant center, transplant type (SLT or DLT), Composite Allocation Score Diagnosis group (A, B, C, or D) or pre-transplant ECMO.

In addition to the patient outcome listed above, the following data will be collected: occurrence of chronic lung allograft dysfunction (CLAD); incidence of major lung events that are determined to be potentially related to the use of LungFX (a major lung event is one or more of the following: acute rejection, bronchial complication, respiratory failure, major pulmonary infection, or re-transplant); grade of Primary Graft Dysfunction (PGD) at 48 hours and 72 hours following transplant; DCD versus DBD status of donor lung; acute rejection within one year (AMR/ACR); “extended” or “standard” criteria lung donor; reason for lung referral for evaluation using LungFX; Patients’ time on transplant list; patients’ Composite Allocation Score Diagnosis Group and pre-transplant ECMO; match run sequence number of recipient; long-term survival status; graft survival; cause of death; P240033 - Michael Roberts Page 4 oxygen requirements at rest; physical capacity; work status; preservation times, including cold ischemic times and perfusion time; proportion of referrals evaluated using LungFX; proportion of referrals placed directly to transplant; proportion of lungs evaluated using LungFX accepted for transplant; proportion of lungs evaluated using LungFX declined for transplant; proportion of lungs received by LBE for evaluation using LungFX that were placed for transplant without the EVLP procedure being performed; and EVLP parameters at end of LungFX procedure for lungs that are accepted for transplant, specifically including: peak airway pressure (PAwP); static and dynamic compliance; pulmonary vascular resistance (PVR); and perfusate gas analysis at lung inflow and outflow, including partial pressure of oxygen (PO_2), pH, glucose, and lactate.

From the date of study protocol approval, LBE must meet the following timelines for patient enrollment in the LungFX PAS:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 18 months
- 50% of subjects enrolled within 36 months
- 100% of subjects enrolled within 54 months

In addition, LBE must submit separate periodic reports on the progress of the LungFX PAS as follows:

- PAS Progress Reports every six months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.

- If any enrollment milestones are not met, LBE must begin submitting quarterly enrollment status reports every three months in addition to the periodic (6-month) PAS Progress Reports, until FDA notifies LBE otherwise.

- Submit the Final PAS Report three months from study completion (i.e., last subject's last follow-up date).

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality Management System (QMSR) regulation (21 CFR 820).

I. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.