SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Portable Ex-Vivo Organ Perfusion System for Donor Lungs Preservation
Device Trade Name:	OCS™ Lung System
Applicant's Name and Address:	TransMedics Inc. 200 Minuteman Road, Suite 302 Andover, MA 01810
Premarket Approval Application (PMA) Number:	P160013
Date of Panel Recommendation:	TBD
Date of Good Manufacturing Practice Inspection:	TBD
Date of Notice of Approval to the Applicant:	TBD
Priority Review:	Granted priority review on May 23, 2016

II. INDICATIONS FOR USE

The TransMedics® Organ Care System™ (OCS) Lung System is a portable organ perfusion, ventilation, and monitoring medical device intended to preserve donor lungs in a near physiologic, ventilated, and perfused state for transplantation.

III. CONTRAINDICATIONS

Moderate to severe donor lung injury with air leak (as seen on radiological studies, bronchial examination or final visual assessment in donor's chest) to avoid:

- Perfusate leakage at injured segments into the airways and potential edema formation
- Inability to recruit donor lungs due to air leak

IV. WARNINGS AND PRECAUTIONS

Refer to the labeling (Clinical User Guide and Technical User Guide) for applicable warnings and precautions.

V. DEVICE DESCRIPTION

The **TransMedics® OCS™ Lung System** consists of the following major components (see Figure 1).

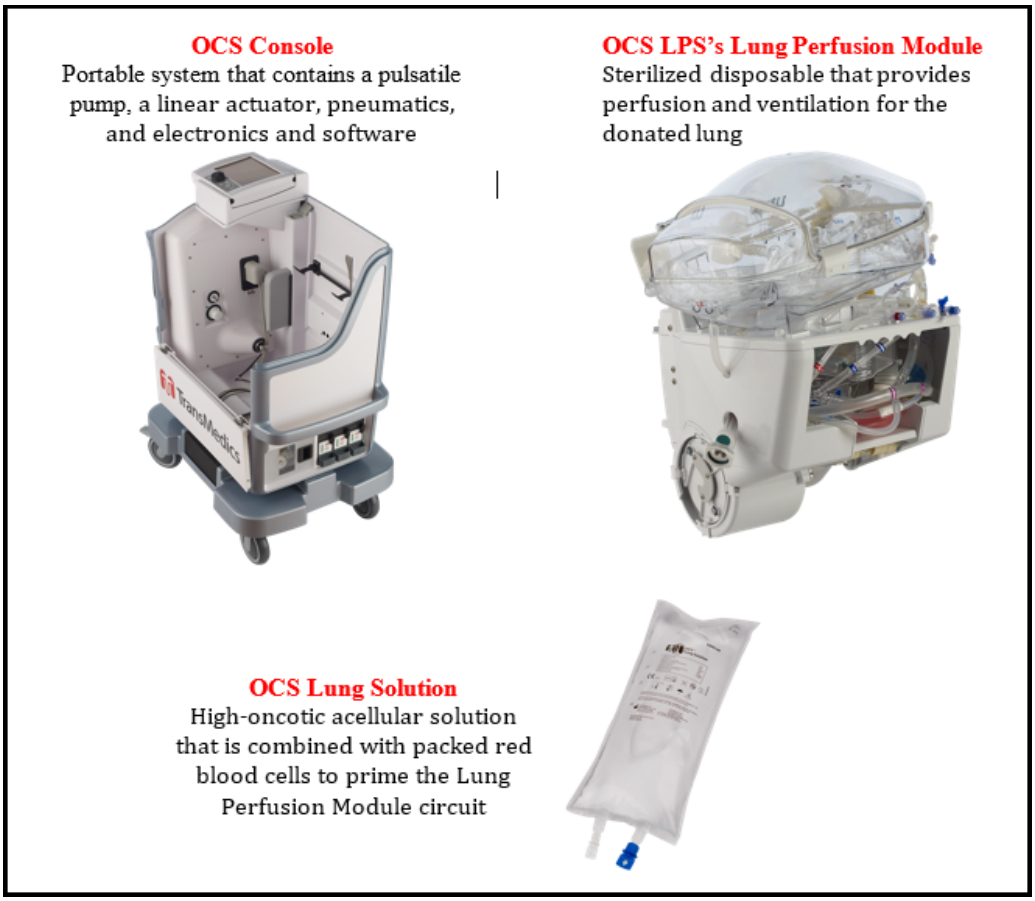
1. **OCS™ Lung Console (Lung Console)**: (b) (4) [redacted]

2. **OCS™ Lung Perfusion Set (LPS):** The LPS consists of:
   - (b) (4) [redacted] Lung Perfusion Module (LPM); and
   - LPS Accessories, (b) (4) [redacted]
     - (b) (4) [redacted]

   The LPM consists of an organ chamber to contain the lungs, tubing, a perfusate reservoir, (b) (4) [redacted]

3. **OCS™ Lung Solution (OCS Lung Solution):** (b) (4) [redacted]

Figure 1: Major Components of OCS Lung System



(b) (4)

(b) (4)

[redacted]

A. Mode of Action

The OCS Lung System performs two primary functions to achieve its intended use: (1) preserving the lung and (2) incorporating monitoring capabilities to assess the organ and its preservation conditions. The scientific rationale supporting the selection of these two fundamental technologies follows.

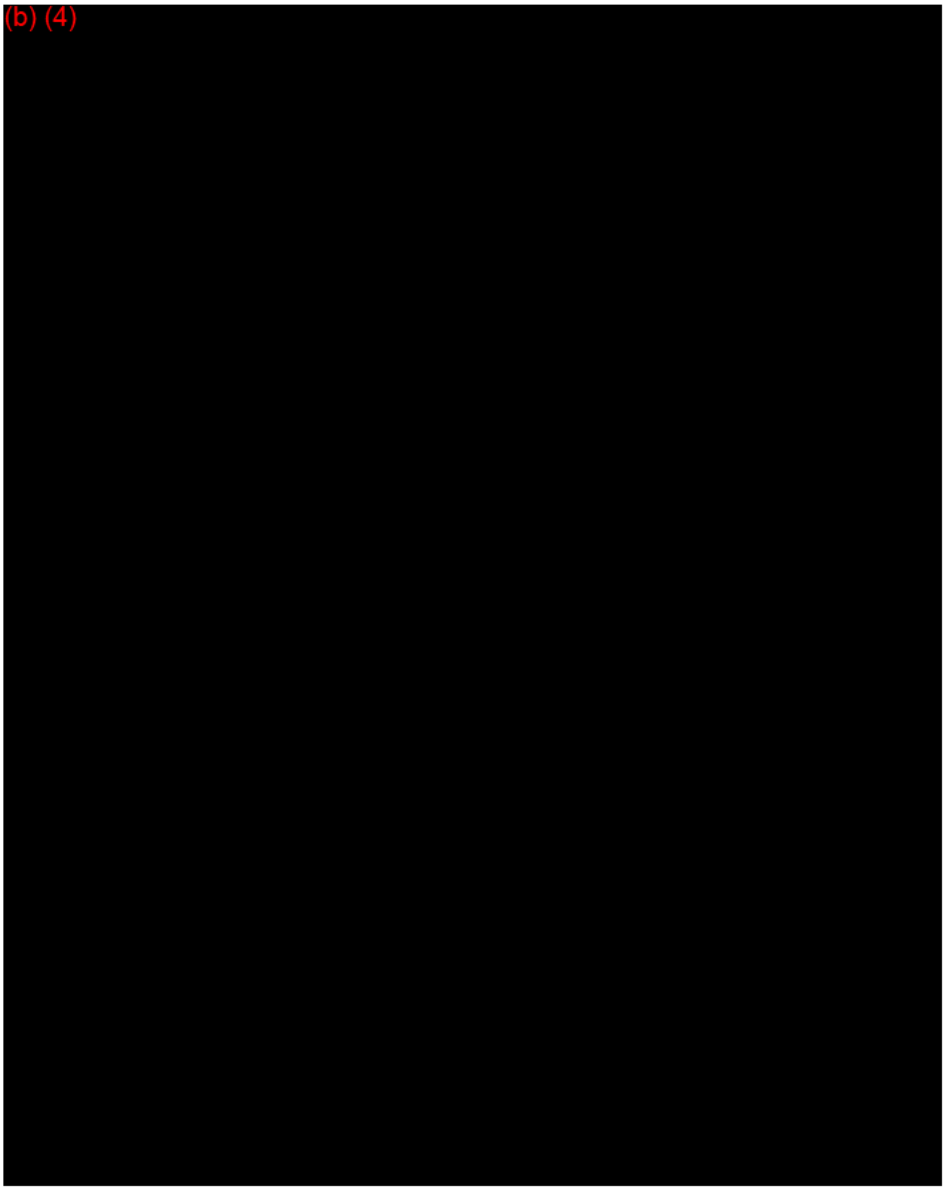
B. Lung Preservation

The OCS Lung System supports and maintains the donated lung function by continuously circulating a warm, oxygenated, blood-based perfusate while ventilating the lung. These features allow the lung to be maintained in a metabolically active state, devoid of damage that would otherwise be caused by cold or warm ischemia. The donated lung is transported in an organ chamber designed specifically to protect the lung and to enable the ventilation and perfusion of the lung.

The OCS Lung System ventilation is (b) (4)

[redacted]

Figure 2: (b) (4)



C. Monitoring Capabilities

The OCS Lung System was specifically designed to provide a means to allow the transplantation team to evaluate the preservation conditions and the function of the organ during transport. The current preservation methods for donor organs (preservation solutions and transport on ice) maintain the organ in a non-functioning state, thereby limiting the ability to evaluate organ function immediately prior to transplantation.

In contrast, the OCS Lung System incorporates a number of sensors to assess organ function and the preservation conditions during transportation. Specifically, it monitors (b) (4)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional procedures used in the preservation of donor lungs are limited to cold, static storage of the donor lung in a hypothermic preservation solution prior to transplantation. Other options are to forgo a lung transplant, which would mean the patient would remain on the transplant waiting list. Certain patients on the transplant waiting listing will either expire while waiting or become too ill to be transplanted.

There are no other legally marketed devices in the US that provide portable ex-vivo perfusion and monitoring of standard criteria donor lungs.

VII. MARKETING HISTORY

TransMedics has not marketed the OCS Lung System in the United States. In December 2011, TransMedics began distribution of the OCS Lung System in the European Union under CE-mark authorization. The OCS Lung System is classified as a Class IIa device under the European Medical Device Directive 93/42/EEC. In addition, the OCS Lung System is commercially available and marketed in Australia. The OCS Lung System has not been withdrawn from marketing for any reason related to the safety and effectiveness of this system.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

There are adverse events associated with lung transplantation. The adverse events that were observed for subjects treated with the OCS Lung System in clinical trials include: respiratory failure; pleural effusion; pneumothorax; hemothorax; bronchostenosis; pulmonary embolism; bronchial secretion retention; chylothorax, acute respiratory failure, diaphragmatic paralysis, emphysema, pulmonary edema, pneumonia; lung infection; bronchopneumonia; infection; bronchitis, lung infection pseudomonal; respiratory tract infection; diverticulitis, aspergillosis;, fungaemia, parainfluenzae virus infection, postoperative wound infection, pseudomonas infection, toxoplasmosis, atrial fibrillation; cardiac arrest; cardiac failure congestive; tachycardia, myocardial ischaemia, pericarditis, right ventricular failure, ventricular fibrillation, acute renal failure; renal failure; hemorrhage; deep vein thrombosis; ischaemia; haemodynamic instability, orthostatic hypotension, shock, post-procedural hemorrhage; wound dehiscence; complications of transplant surgery, procedural complication, drug toxicity, weaning failure, wound complication, impaired gastric emptying, dysphagia, gastrointestinal haemorrhage, large intestine perforations, diarrhea, duodenal perforation, gastric ulcers, gastritis, gastrointestinal disorder, gastrointestinal ulcer hemorrhage, nausea, pancreatitis, lung transplant rejection; cerebrovascular accident; encephalopathy, brain edema, convulsion, cerebellar ischaemia, cerebral infarction, hypoxic encephalopathy, chest pain, impaired healing, leukopenia, coagulopathy, hyponatremia, myopathy, rhabdomyolysis, mechanical ventilation, transfusion, pyloric stenosis, antibiotic resistant staphylococcus test positive, angioedema.

Potential AEs that may occur but that were not observed in the INSPIRE study include: anemia, cough, gastroesophageal reflux disease, malignancy (post-transplant lymph proliferative disorder (PTLD)), mucus plug, neurological dysfunction, pleural bleeding and pulmonary infarction.

IX. SUMMARY OF PRECLINICAL STUDIES

TransMedics has performed a series of studies to demonstrate the OCS Lung System meets its performance specifications and that it demonstrates a reasonable assurance of safety and effectiveness. The following testing is summarized in this section: (A) engineering bench testing; (B) biocompatibility; (C) software verification and validation; (D) electrical safety and EMC; (E) sterilization and shelf life; and (F) animal functional studies.

A. Engineering Bench Testing

Testing was performed to evaluate:

- Mechanical bench testing of the OCS Lung System
- Mechanical bench testing of the Lung Console
- Mechanical bench testing of the LPS

Some of the tests were performed on earlier designs of the device. In such cases, the testing remains valid and representative of the design for which clearance is sought because the incremental design changes were unrelated to the function and specification under evaluation in that test.

In addition, some of the tests provided were performed in support of the OCS Heart System. The OCS Heart System and the OCS Lung System share the same fundamental design concepts and, in fact, some of the components or assemblies are identical between the systems. The OCS Heart System testing included in this section involved components or assemblies that are identical to those in the OCS Lung System. Accordingly, this testing is considered fully appropriate and applicable in support of the subject PMA.

B. Biocompatibility

TransMedics performed a series of biocompatibility studies to demonstrate the safety, suitability, and compatibility of the materials of the TransMedics LPS, which consists of the LPM and LPS Accessories. These studies were selected and performed in consultation with international recognized safety standards. All studies cited here were conducted in compliance with 21 CFR Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies (GLPs).

The LPS has been categorized for its body contact and duration of contact according to ISO 10993-1, Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing, to select the appropriate biocompatibility testing program. Biocompatibility tests and results are provided in Table 2 below.

Table 2: Biocompatibility Testing Summary for LPS

Biocompatibility Test	Results
Cytotoxicity Test	Non-cytotoxic
Sensitization (2 extracts)	No delayed dermal contact sensitization
Intracutaneous Reactivity (2 extracts)	No irritation
Acute Systemic Toxicity (2 extracts)	No systemic toxicity observed
Pyrogenicity – Material Mediated	Non-pyrogenic

Biocompatibility Test	Results
Pyrogenicity – Bacterial Endotoxin	Non-pyrogenic
In Vitro Hemolysis	Non-hemolytic
Genotoxicity – Bacterial Reverse Mutagen Study (2 extracts)	Non-mutagenic
Genotoxicity – Mouse Lymphoma Assay (2 extracts)	Non-mutagenic
Genotoxicity – Mouse Peripheral Blood Micronucleus (2 extracts)	Non-mutagenic
USP Physicochemical Tests • Non-volatile residue • Residue on Ignition • Heavy Metals • Buffering Capacity	Meets USP limits; no significant extractables

Additional biocompatibility testing has been performed on the OCS Lung Solution including the OCS Lung Solution bag. The testing and results are summarized in Table 3 below.

Table 3: Biocompatibility Testing of OCS Lung Solution and Bag

Biocompatibility Test	Results
Cytotoxicity Test	Non-cytotoxic
Sensitization	No delayed dermal contact sensitization
Intracutaneous Reactivity	No irritation
Acute Systemic Toxicity	No systemic toxicity observed
Pyrogenicity – Material Mediated	Non-pyrogenic
Pyrogenicity – Bacterial Endotoxin	Non-pyrogenic
In Vitro Hemolysis	Non-hemolytic

The safety and suitability of the OCS Lung Solution has also been evaluated. All materials used in the manufacture of the OCS Lung Solution meet compendial requirements; thus, they are suitable and safe for their intended use. In addition, the chemical properties of the packaging bag were evaluated to ensure their chemical suitability for the intended use of solution storage. The bag materials successfully passed the testing, demonstrating its suitability and safety as the primary storage container for the OCS Lung Solution.

C. Software Verification and Validation

TransMedics performed system level software verification and validation testing to demonstrate the OCS Lung System performs as intended. The device passed all testing, met its requirements, and is safe, suitable and ready for commercial distribution. Software documentation has been provided in accordance with the FDA guidance document entitled "Guidance for the Contents of Premarket Submissions for Software Contained in Medical Devices," dated May 11, 2005.

Verification and validation testing included unit tests, system level verification tests (which included functional testing to demonstrate the device meet its requirements), code review, and validation testing.

D. Electrical Safety and EMC

1. Electrical and Medical Device Safety

The OCS Lung System was tested to demonstrate that it meets the requirements for medical device safety, including electrical safety. The system was tested by an outside laboratory according to the Edition 3.1 of the IEC 60601-1 standard, as well as the ANSI/AMMI and CSA versions of the standard. The OCS Lung System met the requirements of the standards. Results are shown in Table 4 below.

Table 4: Summary of the Test Results for Electrical, Thermal, and Mechanical Safety

Test Description	IEC 60601-1 Clause	Result
General Requirements	4	Pass
General Requirements for Testing ME Equipment	5	Pass
Classification of ME Equipment and ME Systems	6	Pass
ME Equipment, Identification Marking and Documents	7	Pass
Protection Against Electrical Hazards from ME Equipment	8	Pass
Protection Against Mechanical Hazards of ME Equipment and ME Systems	9	Pass
Protection Against Unwanted and Excessive Radiation Hazards	10	N/A
Protection Against Excessive Temperatures and Other Hazards	11	Pass
Accuracy of Controls and Instruments and Protection Against Hazardous Outputs	12	Pass
Hazardous Situations and Fault Conditions	13	Pass
Programmable Medical Electrical Systems (PEMS)	14	Pass
Construction of ME Equipment	15	Pass
ME Systems	16	N/A

2. EMC

The OCS Lung System was tested to demonstrate that it meets the requirements for radio frequency emissions and radio frequency susceptibility (together, EMC). The system was tested by an outside laboratory according to standards for EMC requirements of electrical equipment (IEC 60601-1-2 (4th edition) – Group 1, Class A, non-life supporting equipment, CISPR 25, and RTCA DO-160G). The OCS Lung System met the requirements of the standards. Results are shown in Table 5 below.

Table 5: Summary of the Emission and Immunity Testing for OCS Lung System

Test	Standard	Test Level	Results
Radiated Emissions	CISPR 11	Group 1, Class A	Pass
AC Mains Conducted Emissions	CISPR 11	Group 1, Class A	Pass
Harmonics Emissions	IEC 61000-3-2	Class A	Pass
Voltage Fluctuation/ Flicker	IEC 61000-3-3	D_{MAX} = 4%	Pass
Electrostatic Discharge Immunity	IEC 61000-4-2	±8 kV Contact ±15 kV Air	Pass
Radiated RF Immunity	IEC 61000-4-3	3 V/m	Pass
Electrical Fast Transients Immunity	IEC 61000-4-4	±0.5 kV, ±1 kV, ±2 kV	Pass
Surge Immunity	IEC 61000-4-5	±0.5 kV, ±1 kV, Line-to-line ±0.5 kV, ±1 kV, ±2 kV, Line-to-PE	Pass
Conducted RF Immunity	IEC 61000-4-6	3 V_{RMS} (AC Mains) 6 V_{RMS} (AC Mains, ISM Bands)	Pass
Power Frequency Magnetic Field Immunity	IEC 61000-4-8	30 A/m, 50 or 60 Hz	Pass
Voltage Dips & Interruptions Immunity	IEC 61000-4-11	> 95% Dip for 0.5 Cycle 60% Dip for 5 Cycles 30% Dip for 25 Cycles > 95% Dip for 5 seconds	Pass
Radiated Emissions, Vehicles Environment	CISPR 25	Class I	Pass
Radiated Emissions, Airborne Environment	RTCA DO-160G	n/a	Pass

E. Sterilization and Shelf Life Testing of the Disposable Components

1. Sterilization

The LPS is sterilized using Ethylene Oxide (ETO). ETO sterilization validation was performed per ISO 11135-1:2007 and demonstrates that the ETO sterilization process and equipment are capable of reliably ETO sterilizing the LPS to a minimum sterility assurance level of 10^{-6}. The lethality of the ETO sterilization process was demonstrated utilizing the overkill concept of sterilization.

Ethylene oxide (ETO) and ethylene chlorohydrin (ECH) residuals were evaluated and determined to be well below the maximum allowable limits of 60 mg (ETO) and 45 mg (ECH)

specified for blood oxygenators and blood separators in ISO 10993-7: 2008, Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals.

OCS Lung Solution is sterilized (b) (4) . The (b) (4) was validated according to (b) (4) Sterilization validation demonstrated a minimum SAL of $\leq 10^{-6}$ for the OCS Lung Solution.

2. Shelf Life Testing

Package integrity and simulated shipping testing was performed for the LPS and OCS Lung Solution to confirm that it can withstand worldwide shipping. Shelf life testing demonstrates the safety and suitability of the (b) (4) Real-time and accelerated shelf life testing supports the safety and suitability of the OCS (b) (4) .

F. Animal Functional Testing

(b) (4)

X. SUMMARY OF CLINICAL STUDIES – INSPIRE STUDY

The primary data set in support of this PMA application is the INSPIRE Trial, which is a randomized, controlled, multi-center study conducted at 21 investigational sites in the U.S., Canada, Australia, and the European Union. The INSPIRE trial was conducted under IDE (b) (4), conditionally approved on October 26, 2011 and fully approved on February 3, 2012.

A. Study Objectives and Endpoints

The primary objective of the INSPIRE study is to compare the safety and effectiveness of the OCS Lung System with the current cold ischemic storage standard of care for the preservation of standard criteria donor lungs. INSPIRE is a prospective, multi-center, randomized, controlled non-inferiority study with patients assigned to either the standard cold static organ preservation (control) or to the OCS Lung System (treatment).

Follow-up data collection was conducted throughout the first 72 hours, at hospital discharge, 30 days, and 6 months post-transplant, with additional long-term data collection at 12 and 24 months.

B. Primary Effectiveness Endpoint

The primary endpoint of the INSPIRE trial was a composite of patient survival day 30 post-transplantation, and absence of ISHLT Primary Graft Dysfunction (PGD) Grade 3 (PGD3) within the first 72 hours (T72) post-transplantation.

INSPIRE was designed as a non-inferiority study, with a non-inferiority margin of 4.0%, and it was pre-specified that in the event non-inferiority is demonstrated, superiority will be tested using Chi-square test or, in the case of one or more cells of contingency table having an expected frequency of five or less, Fisher's exact test (two-sided).

1. ISHLT PGD Grading

The INSPIRE Trial protocol, investigative sites, and the independent Medical Monitor followed the ISHLT Consensus Statement that was published in 2005 (Christie, et al. 2005) for grading PGD as described below:

- If patient is extubated, then PGD is graded as 0 or 1 depending on absence or presence of infiltrates and/or edema assessed by chest x-ray, respectively.
- If patient is intubated, then PaO_2/FiO_2 ratio is considered for grading PGD as follows:
  - PaO_2/FiO_2 Ratio:
    - <200 mmHg = PGD3
    - 200-300 mmHg = PGD2
    - >300 mmHg = PGD Grade 0 or Grade 1, depending on absence or presence of infiltrates and/or edema assessed by chest x-ray, respectively
- If extracorporeal membrane oxygenation (ECMO) was used post-transplantation for graft dysfunction, then the PGD grade would be assigned as Grade 3 regardless of ventilation status.

In a few cases in the INSPIRE trial, centers used their standard-of-care protocols for using prophylactic ECMO inserted prior to transplantation for management of pulmonary hypertension patients (Tudorache et al. 2015; Ius et al. 2016), or for better hemodynamic management to

protect cardiac function during the early post-transplant period. Prophylactic ECMO was not for oxygenation support of the recipient; therefore, these patients were graded according to the PGD grading rules above (assessing intubation status, PaO_2/FiO_2 ratio, and chest x-ray). All these patients were reviewed and adjudicated by the blinded independent Medical Monitor.

C. Secondary Effectiveness Endpoints

The secondary effectiveness endpoints were:

- Incidence of ISHLT PGD3 at T72 hours post-lung transplantation
- Incidence of ISHLT PGD2 or 3 at T72 hours post-lung transplantation
- Patient survival at day 30

D. Other Clinical Endpoints

Other clinical endpoints defined in the protocol were:

- Incidence of PGD3 within the first 72 hours post-lung transplantation
- Incidence of PGD3 or 2 within the first 72 hours post-lung transplantation
- Composite of all cause patient survival at day 30 and absence of ISHLT PGD Grade 2 or 3 in the first 72 hours
- Composite of all cause patient survival at initial hospital discharge and absence of ISHLT PGD Grade 2 or 3 in the first 72 hours
- PGD score at T0, T24, and T48 hours
- Duration of invasive mechanical ventilation
- Length of post-transplant ICU stay
- Length of post-transplant hospital stay
- Additional hospital admission post initial discharge

E. Safety Endpoint

The safety endpoint was the mean number of lung graft-related serious adverse events (SAE) through the 30 days post-transplantation per subject. A lung graft-related serious adverse event was defined as the occurrence of any of the following four categories of adverse events that are also serious. In calculating the primary safety endpoint, multiple occurrences of SAE of the same category on the same subject within 30 days was counted as one lung graft-related SAE.

- Acute rejection
- Respiratory failure
- Bronchial anastomotic complication
- Major pulmonary-related infection

F. Study Population

Subjects were lung transplant recipients who met inclusion/exclusion criteria as outlined below. Inclusion/exclusion criteria were also defined for the donor organs as described below.

Inclusion Criteria:

Donor Inclusion Criteria

- Age <65 years old
- Normal gas exchange, i.e., $PaO_2/FiO_2 \geq 300$, at the time of final acceptance of donor lungs
- No active primary pulmonary disease
- Donor lungs suitable for preservation with either OCS or Standard of Care

Recipient Inclusion Criteria:

- Registered male or female primary double-lung transplant candidate
- Age ≥ 18 years old
- Signed: (1) written informed consent document and (2) authorization to use and disclose protected health information

Exclusion Criteria:

Donor Exclusion Criteria

- Positive serology for Hepatitis B, Hepatitis C, or HIV
- Presence of moderate to severe traumatic lung injury presenting as moderate or massive pneumothorax, hemothorax or lung contusion as evidenced by chest X-ray, CT-Scan, visual inspection or bronchoscopy
- Presence of confirmed active pneumonia

Recipient Exclusion Criteria

- Prior solid organ or bone marrow transplant
- Single lung recipient
- Multiple organ transplant recipient
- Chronic use of hemodialysis or diagnosis of chronic renal insufficiency

G. Study Treatments

The donor organs in the OCS arm were perfused with the OCS Lung System. The control arm utilized an FDA-cleared, commercially available Low Potassium Dextran (LPD) solution, for lung flushing and preservation. The solution was used according to its instructions for use.

H. Analysis Populations

The primary analysis of effectiveness was based on the PP population consisting of all randomized patients who are transplanted and have no major protocol violations and for whom the eligible donor lung received the complete preservation procedure as per the randomization assignment.

A secondary analysis of effectiveness was based on the modified ITT (mITT) population consisting of all randomized patients for whom a matching donor lung has been harvested and determined to be eligible for preservation with either OCS or Control before any attempt has been made to preserve the lung with either OCS or Control.

Safety analyses were based on the Safety Population (SP), consisting of all patients who were transplanted in the trial with eligible donor lungs that had been preserved with OCS or Control,

except for patients randomized to OCS who, due to a decision of the treatment team, were switched to standard therapy before OCS treatment is initiated.

I. Statistical Analysis - Effectiveness

The primary effectiveness endpoint was analyzed by calculating the one-sided 95% upper confidence limit based on the normal approximation for the difference in proportions. An upper confidence limit less than the non-inferiority margin of 0.04 was required to demonstrate non-inferiority of OCS to Control for the primary effectiveness endpoint. In the event non-inferiority was demonstrated, a Chi-square test (or Fisher's exact test, as appropriate) was to be used to test for superiority

The secondary effectiveness endpoints for this study were tested using a fixed sequence testing procedure to control the type-I error rate as follows:

- Incidence of ISHLT PGD Grade 3 at 72 hours post-lung transplantation (evaluated at a non-inferiority margin of 0.05)
- Incidence of ISHLT PGD Grade 2 or 3 at 72 hours post-transplantation (evaluated at a non-inferiority margin of 0.075)
- Patient survival at Day 30 (evaluated at a non-inferiority margin of 0.04)

The secondary effectiveness endpoints were analyzed by calculating the one-sided 95% upper confidence limit based on the normal approximation for the difference in proportions. An upper confidence limit less than the secondary endpoint's respective non-inferiority margin was required to demonstrate non-inferiority of OCS to Control. In the event non-inferiority was demonstrated, Chi-square test (or Fisher's exact test, as appropriate) was to be used to test for superiority.

Because fixed sequence testing was used for the secondary effectiveness endpoints, no adjustment for the multiplicity of these endpoints needed to be made.

All endpoints will be presented as:

- OCS Arm (lungs perfused on OCS Lung System with either OCS Solution or commercially available LPD solution) vs. Control; and
- OCS Solution (lungs perfused on OCS Lung System with OCS Solution only) vs. Control.

J. Statistical Analysis – Safety

The primary safety endpoint was analyzed using a one-sided two-sample t-test at a non-inferiority margin of 0.07 events. If non-inferiority was demonstrated, a corresponding (two-sided) two-sample t-test for superiority was to be performed.

Other safety evaluations are reported using frequencies and percentages.

K. Randomization

Subjects were allocated with equal probability (1:1) to OCS and CONTROL arm using block randomization stratified by site with a block size of 8. In the case of donor screen failure, recipients were returned to the waiting list with the original randomization assignment.

L. Study Assessments

Table 6 and Table 7 describe the schedules of assessments for donors and recipients, respectively.

Table 6: Schedule of Assessments for Donors

Evaluations	Screening & Acceptance	Control	OCS Preservation
Organ ID	X		
Demographics/Characteristics	X		
Eligibility	X		
Donor Cause of Death	X		
Donor History/Lifestyle Factors (smoking history)	X		
Medical History	X		
Final Blood Gas and PaO_2/FiO_2 Ratio at Acceptance of the Lungs	X		
Hemodynamics	X		
Ventilation Settings at Final Blood Gas	X		
Final Chest X-ray report/findings	X		
Final Bronchoscopy findings	X		
Cross clamp time and flush detail		X	X
OCS Pre-Instrumentation ABG			X
OCS Instrumentation Details			X
OCS Monitoring Observations			X
OCS Preservation Parameters			X
Device Malfunction (if applicable)			X
Non-transplant Reasons (if applicable)		X	X

Table 7: Schedule of Assessments for Recipients

Evaluations	Prior to or on Day of Tx	T 0	T 24	T 48	T 72	Day 7	Dis-charge	Day 30	Mo 6	Mo 12	Mo 24
Randomization	X										
Informed Consent	X										
Organ ID	X										
Demographics/ Characteristics	X										
Eligibility	X										
Etiology of Lung Failure	X										
Medical History	X										
Pulmonary Assessments	X						X				
Cardiac History	X										
Prior Sternotomy/Thoracotomy	X										
Transplant Details	X										
Graft Surveillance		X	X	X	X						
Primary Graft Dysfunction Scores		X	X	X	X						
Patient Survival								X	X	X	X
Graft Survival								X	X	X	X
Chest X-Ray		X	X	X	X		X				
Hemodynamics	X	X	X	X	X						
Immunosuppressive Induction	X										
Immunosuppressive Therapy						X	X				
Pre-op treatment (prostaglandins, iNO)	X										
Fluid Balance (I/O)	X	X	X	X	X						
Post-Transplant Hospital/ICU Stay		X	X	X	X	X	X	X	X		
Adverse Events		X	X	X	X	X	X	X			
Lung Related SAEs								X	X		
Bronchoscopy. BAL & Biopsy							X		X*	X*	X*
Pulmonary Function Test							X		X*	X*	X*
Diagnosis of BOS									X	X	X
Mechanical Circulatory Support	X	X	X	X	X	X	X	X			
Invasive Ventilator Support	X	X	X	X	X	X	X	X			
Medications relating to treatment of SAEs Only		X	X	X	X	X	X	X			

* Tests regularly scheduled per center standard of care or performed due to a clinical cause at these timepoints will be collected.

M. Investigational Sites

The INSPIRE study was conducted at 21 sites in the United States, Canada, Europe, and Australia.

N. Patient Cohorts

1. Administrative Extension

The OCS Lung System requires the use of a high-oncotic perfusion solution supplemented with type matched packed red blood cells (pRBCs) as the perfusate mix to perfuse donor lungs with during preservation. The initial OCS Lung INSPIRE Trial IDE was approved to allow for either OCS Lung Solution or a commercially available Low-Potassium Dextran (LPD) solution due to their similar chemical composition. TransMedics' intent was for the OCS Lung Solution to be used exclusively for the duration of the INSPIRE Trial after its approval. However, during the course of the INSPIRE Trial, TransMedics experienced a shortage of the OCS Lung Solution as it was transitioning from one contract manufacturer to another. During this time, many of the INSPIRE investigational sites used LPD solution exclusively.

TransMedics then received several comments from trial investigators indicating that they have observed more lung edema using the LPD solution. TransMedics informed the FDA of this observation and explored several alternatives as to how to present the information in the PMA and on the device labeling. To allow time for continued discussion, TransMedics requested an administrative extension to enroll additional patients beyond the pre-specified total sample size for the INSPIRE Trial to avoid trial stoppage. FDA granted the extension and an additional N=29 subjects were enrolled and transplanted in an "Administrative Extension."

The results of both the pre-specified trial population (INSPIRE Cohort, N=320) as well as the results for the INSPIRE cohort combined with the Administrative Extension ("Combined Cohort") are presented. For simplicity, most of the secondary analyses are presented only for the Combined Cohort.

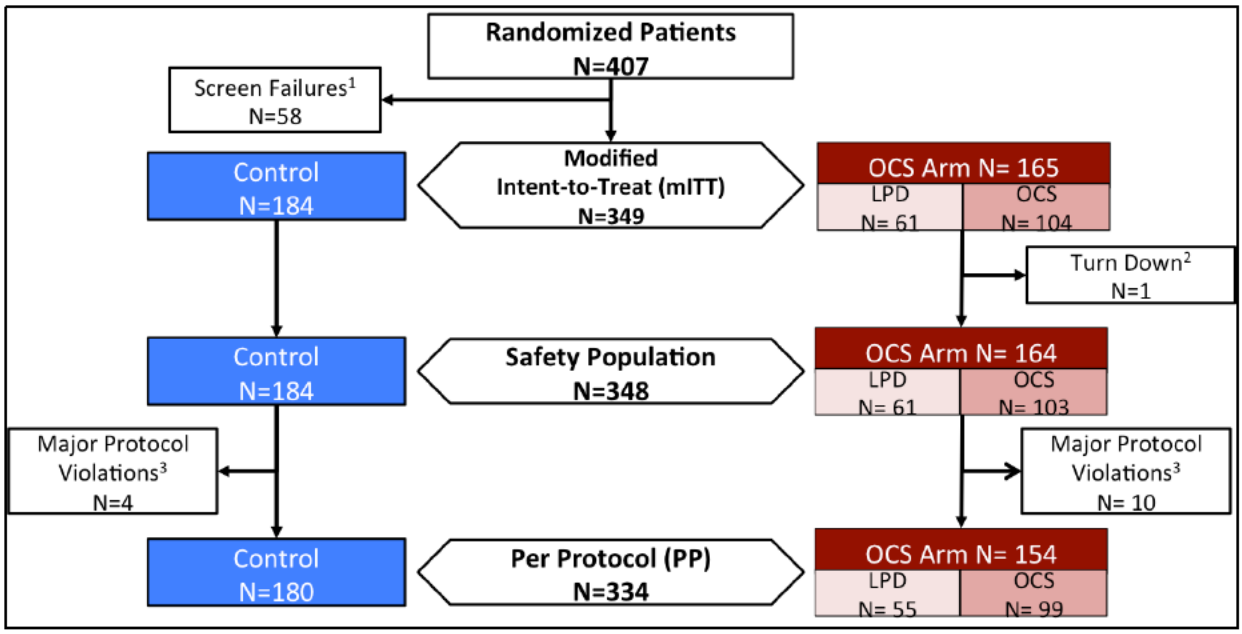
There were 3 key analysis populations pre-specified in the INSPIRE trial:

- **Per-Protocol (PP)**: This population consists of all randomized patients who are transplanted and have no major protocol violations and for whom the eligible donor lung received the complete preservation procedure as per the randomization assignment. (b) (4) [redacted]).
- **Modified Intention-to-Treat (mITT)**: This population consists of all randomized patients for whom a matching donor lung has been harvested and determined to be eligible for preservation with either OCS or Control before any attempt has been made to preserve the lung with either OCS or Control
- **Safety Population (SP)**: This population consists of all patients who were transplanted in the trial with an eligible donor lung that had been preserved with OCS or Control, except for patients randomized to OCS who, due to a decision of the

treatment team, were switched to standard therapy before OCS treatment was initiated.

The subject consort diagram is shown in Figure 3, along with an explanation of the protocol deviations and screen failures.

Figure 3: INSPIRE Trial Enrollment Detailed Consort Diagram



[1] Screen Failures:

- Donor screen failure= 41 (31 OCS, 10 Control)
- Recipient screen failure= 6 (2 OCS, 4 Control)
- Logistics screen failure=11 (10 OCS, 1 Control)

[2] (b) (4) [redacted]

[3] OCS Major Protocol Violations N=10:

- N=1 Donor lung did not meet eligibility criteria due to presence of active pneumonia at time of lung retrieval
- N=1: Donor lung eligibility for the study was not confirmed given that no final donor PaO_2/FiO_2 ratio was obtained during final assessment of the donor prior to retrieval
- N=-1: Donor lung did not meet eligibility criteria due to presence of left lower lobe pneumonia, consolidation and with mucopurulent secretions at time of lung retrieval
- N=1: Donor lung did not meet eligibility criteria due to presence of severe emphysema/COPD with blebs and large ruptured bullae on donor lungs
- N=1: Failure to follow the study protocol for using ABO compatible pRBCs. The donor lungs were perfused using ABO incompatible pRBCs
- N=1: Failure to follow the IFU by exceeding recommended range of OCS pump flow during perfusion of donor lungs, which may have resulted in air being introduced to the perfusion line
- N=1: Failure to follow the IFU and protocol by failing to connect the OCS ventilator air-line to the OCS ventilator circuit to ventilate the donor lungs on the device. Lung was immediately removed from OCS and transplanted using cold storage
- N=1: Failure to follow IFU and protocol for connecting the LPM to engage with the ventilator arm, resulting in interruption of ventilation to the donor lung. Lung was immediately removed from OCS and transplanted using cold storage
- N=1: Failure to follow IFU and protocol for management of donor lung on OCS:

- Staff at investigational site initiated OCS procurement against instructions from sponsor due to his lack of knowledge on how to operate the OCS. The operator was unable to locate the on-button for the OCS device;
- Did not apply the OCS lung wrap to protect against barotrauma;
- Did not perform any blood gas measurements on the OCS to assess the donor lung management

- N=1: Failure to follow IFU for management of donor lung on OCS:
  - Used only 1 liter of perfusion solution instead of minimum of 1.5 liters to prime OCS
  - Did not apply the OCS lung wrap to protect against barotrauma while ventilating donor lungs on OCS

[4] Control Arm Major Protocol Violations N=4:

- N= 3: The donor lungs were flushed and preserved using a different preservation solution than the pre-specified solution in the protocol.
- N=1: Donor lung did not meet eligibility criteria due to presence of active pneumonia/aspiration with mucopurulent secretions in the right and left bronchi at time of harvest.

O. Demographic and Baseline Information

Recipient characteristics are shown in Table 8 below. The two groups were similar in all categories and no significant differences were noted.

Table 8: Recipient Demographic and Baseline Characteristics (mITT Population, N=349, Combined Cohort)

Parameter	Control (N=184)	OCS Arm (N=165)	OCS Solution Subgroup (N=104)
Age (years)			
N	184	165	104
Mean ± SD	50.34 ± 13.43	50.45 ± 12.82	49.63 ± 13.21
Median	55.0	54.0	52.5
Minimum - Maximum	18.0 - 72.0	18.0 - 72.0	18.0 - 71.0
Gender			
Female	35.9% (66/184)	47.9% (79/165)	51.0% (53/104)
Male	64.1% (118/184)	52.1% (86/165)	49.0% (51/104)
Ethnicity			
Hispanic or Latino	9.2% (17/184)	13.3% (22/165)	12.5% (13/104)
Not Hispanic or Latino	70.7% (130/184)	66.7% (110/165)	68.3% (71/104)
Not Applicable	20.1% (37/184)	20.0% (33/165)	19.2% (20/104)
Race			
American Indian or Alaskan Native	0.0% (0/183)	0.0% (0/162)	0.0% (0/102)
Asian	1.6% (3/183)	1.9% (3/162)	1.0% (1/102)
Black or African American	2.7% (5/183)	4.3% (7/162)	4.9% (5/102)
Hispanic	3.3% (6/183)	7.4% (12/162)	5.9% (6/102)

Parameter	Control (N=184)	OCS Arm (N=165)	OCS Solution Subgroup (N=104)
Native Hawaiian or Other Pacific Islander	0.5% (1/183)	0.0% (0/162)	0.0% (0/102)
White	88.0% (161/183)	84.6% (137/162)	87.3% (89/102)
Other	3.8% (7/183)	1.9% (3/162)	1.0% (1/102)
Weight (kg)			
N	184	165	104
Mean ± SD	68.78 ± 15.30	67.13 ± 16.65	65.20 ± 17.35
Median	68.0	66.0	63.0
Minimum - Maximum	37.0 - 112.5	32.0 - 128.0	32.0 - 128.0
Type of Status			
Urgent	84.3% (43/51)	82.7% (43/52)	82.4% (28/34)
High-Urgent	15.7% (8/51)	17.3% (9/52)	17.6% (6/34)
Lung Allocation Score			
N	125	107	66
Mean ± SD	47.57 ± 18.34	50.54 ± 20.10	48.32 ± 17.75
Median	40.0	41.0	40.0
Minimum - Maximum	29.0 - 95.0	29.0 - 95.0	31.0 - 94.0
Primary Cause of Lung Failure			
Chronic Obstructive Pulmonary Disease	28.8% (53/184)	28.5% (47/165)	29.8% (31/104)
Cystic Fibrosis	23.4% (43/184)	20.6% (34/165)	23.1% (24/104)
Idiopathic Pulmonary Arterial Hypertension	4.3% (8/184)	8.5% (14/165)	9.6% (10/104)
Bronchiectasis	4.9% (9/184)	4.8% (8/165)	4.8% (5/104)
Idiopathic Pulmonary Fibrosis	34.8% (64/184)	35.2% (58/165)	32.7% (34/104)
Sarcoidosis	4.9% (9/184)	2.4% (4/165)	1.9% (2/104)
Other	3.3% (6/184)	4.8% (8/165)	2.9% (3/104)
Additional Risk Factors			
Diagnosis of Secondary Pulmonary Hypertension	32.2% (59/183)	40.2% (66/164)	39.8% (41/103)
Diagnosis of Heart Failure	7.2% (13/180)	8.5% (14/164)	11.7% (12/103)

Donor demographic baseline characteristics and risk factors are shown in Table 9 below. The donor characteristics were generally similar between the arms, although there was a trend towards slightly more males than females in the control group. Also, the OCS group had a higher percentage of abnormal findings on final physical examination of the donor lungs prior to retrieval and a higher percentage of surgical complications during retrieval prior to preservation (e.g., adhesions tears, COPD blebs resections).

Table 9: Donor Demographic and Baseline Characteristics (mITT Population, N=349, Combined Cohort)

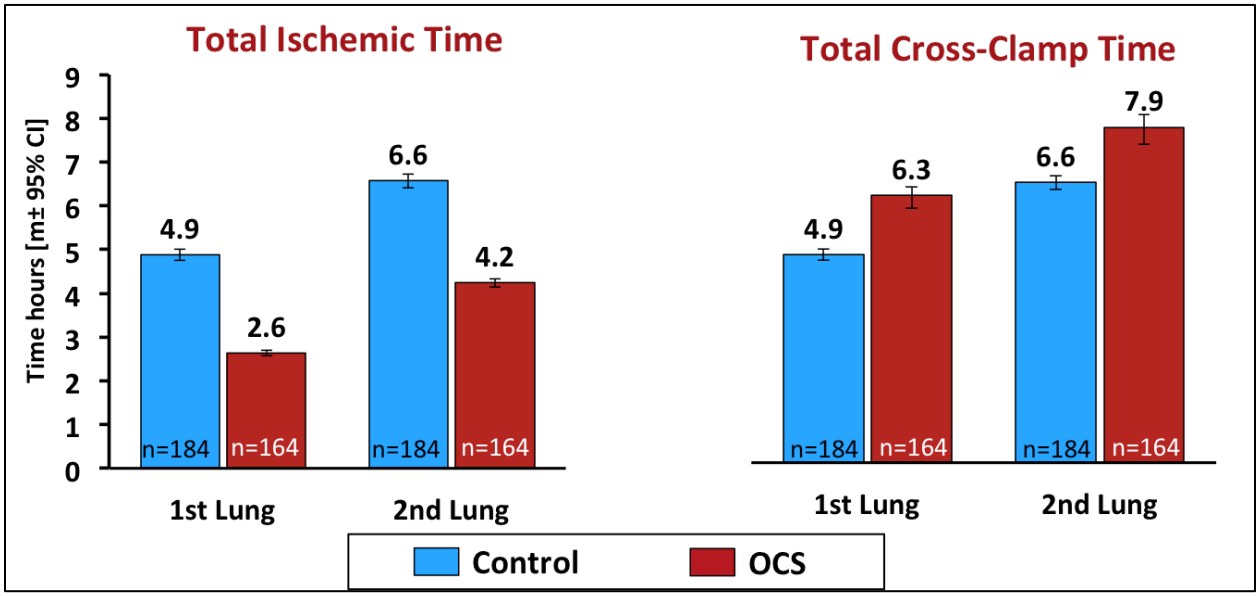
Parameter	Control (N=184)	OCS Arm (N=165)	OCS Solution Subgroup (N=104)
Donor Age (years)	n=183	n=163	n=103
Mean ± SD	40.15 ± 13.70	41.52 ± 14.40	41.00 ± 14.53
Median	42.0	44.0	43.0
Min.-Max.	14.0 - 63.0	13.0 - 64.0	13.0 - 63.0
Gender	n=184	N=165	N=104
Female	39.7% (73/184)	47.3% (78/165)	51.0% (53/104)
Male	60.3% (111/184)	52.7% (87/165)	49.0% (51/104)
Donor Final PaO_2/FiO_2 Ratio	n=184	n=163	n=103
Mean ± SD	431.73 ± 73.34	441.37 ± 78.89	445.83 ± 78.61
Median	427.1	435.0	443.1
Min.-Max.	301.0 - 642.0	304.0 - 689.0	315.0 - 689.0
Abnormal Findings on Physical Examination of Donor Lungs Prior to Retrieval	25.5% (47/184)	36.4% (60/165)	41.3% (43/104)
Any Surgical Complications/Tears during Retrieval?	1.4% (2/148)	6.0% (9/151)	6.3% (6/95)
Cigarette use (>20 pack years) Continued in Last 6 months	n=183	n=164	n=104
Yes	17.5% (32/183)	18.3%(30/164)	18.3% (19/104)
No	71.6% (131/183)	69.5% (114/164)	71.2% (74/104)
Unknown	10.9% (20/183)	12.2% (20/164)	10.6% (11/104)

P. Donor Lung Preservation Characteristics & Critical Times

Donor Lung cross clamp and ischemic times are shown in Figure 4 below. Note that cross-clamp time is the time from aortic cross clamp application time in the donor to the pulmonary artery (PA) cross-clamp removal in the recipient. For the Control group, the total ischemic time is also the cross-clamp time. However, for the OCS group, the total ischemic time is the cross-clamp time **minus** the OCS perfusion time. This explains the differences in total ischemic time.

The use of OCS reduced the injurious ischemic time on the donor lungs while allowing donor lungs to be preserved with a significantly longer cross clamp time.

Figure 4: **Ischemic and Cross-Clamp Time for OCS and Control groups (Combined Cohort, OCS Group N= 165, Control Group N = 184)**

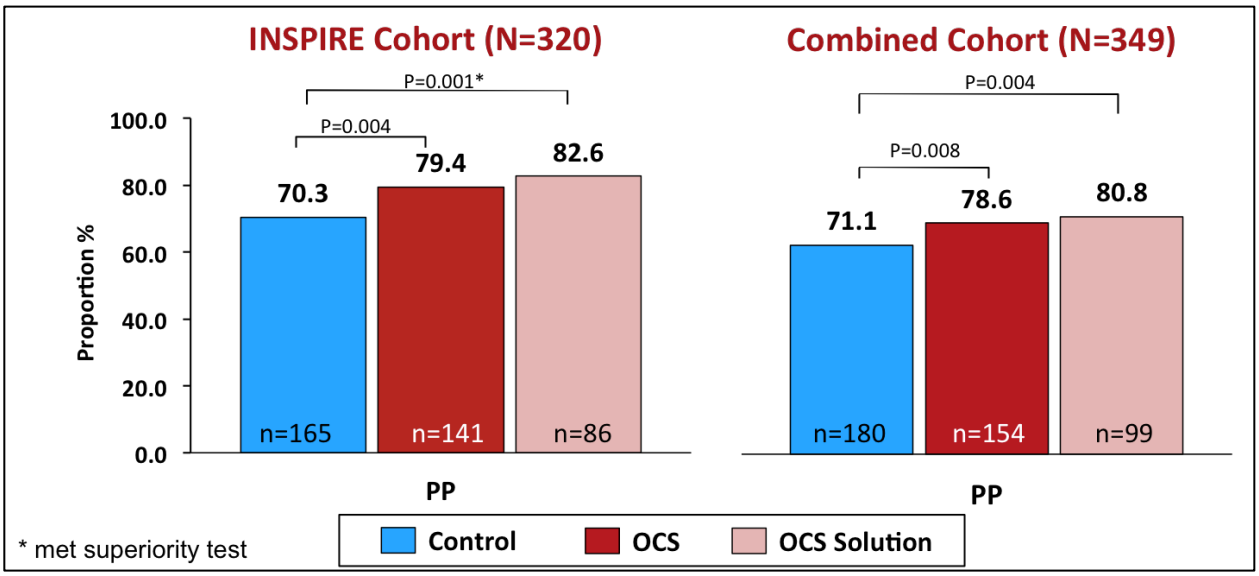


Q. Primary Endpoint

The INSPIRE Trial primary effectiveness endpoint assessed the impact of the OCS Lung System on 30-Day patient survival and incidence of the most severe form of PGD3 within 72 hours post-transplantation.

As shown in Figure 5 below, the primary effectiveness objective was met in the INSPIRE Cohort (N=320) as well as in the Combined Cohort (N=349), which includes patients from the Administrative Extension. The rate of the primary endpoint in the OCS arm was non-inferior to Control arm at the 4% non-inferiority margin in the PP population, the primary analysis population for the INSPIRE trial (p=0.008 and p=0.004 for the Combined and INSPIRE Cohorts, respectively). The primary effectiveness objective was also met in the OCS Solution subgroup in both populations, which reflects results of the OCS Lung System under review in this PMA as well as the to-be-marketed product. In the ITT population, the OCS arm narrowly missed the non-inferiority margin for both Cohorts (p=0.06 and p=0.10), while the OCS Solution subgroup was shown to be statistically non-inferior in both Cohorts (p=0.012 and p=0.033 for the Original and Combined Cohorts, respectively).

Figure 5: Primary Effectiveness Endpoint Results for PP Population for INSPIRE Cohort (N=320) and Combined Cohort (N=349)



R. 30-Day Survival

As shown in Figure 6 below, patient survival at 30 days is lower in the OCS arm in comparison to control. As shown in Figure 7 below, of the 11 deaths in the OCS arm, 3 were due to cardiac causes, 3 were due to vascular causes, 4 were due to lung graft failure or graft infection and 1 was due to sepsis. The death in the control group was due to metabolic coma.

Note that the nationwide average 30-day all-cause mortality reported for lung transplant recipients in the 2012 OPTN/SRTR annual report was 4.1% (OPTN/SRTR 2014). The rate reported for the OCS group (6.7%) is similar to the national average while the control group mortality is lower (0.5%).

Figure 6: Survival at 30 Days in the INSPIRE Trial

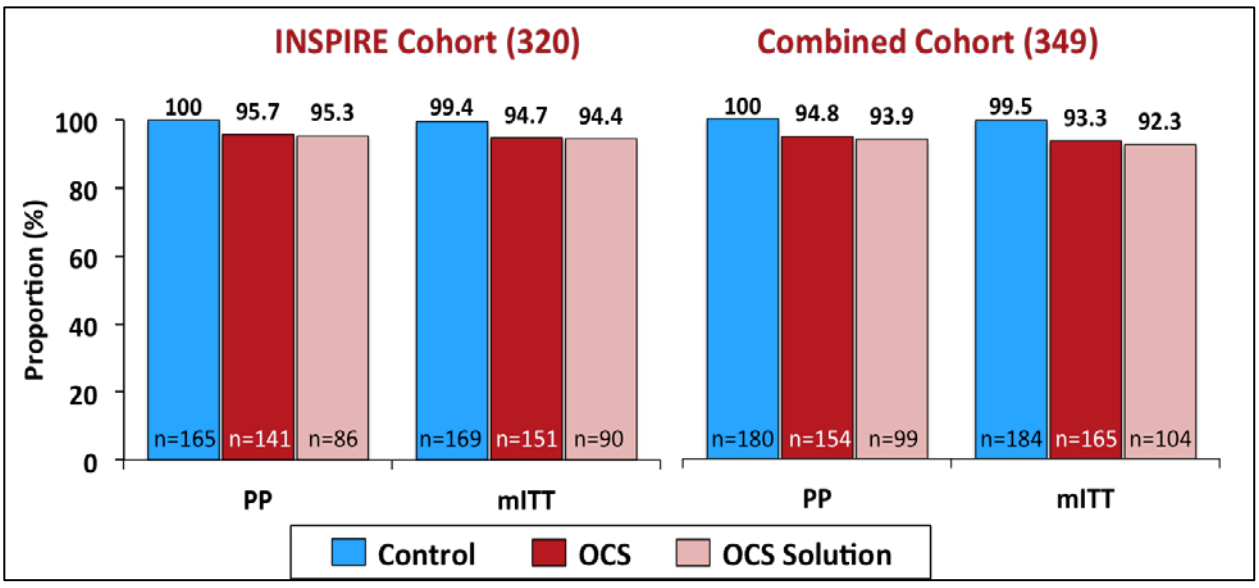
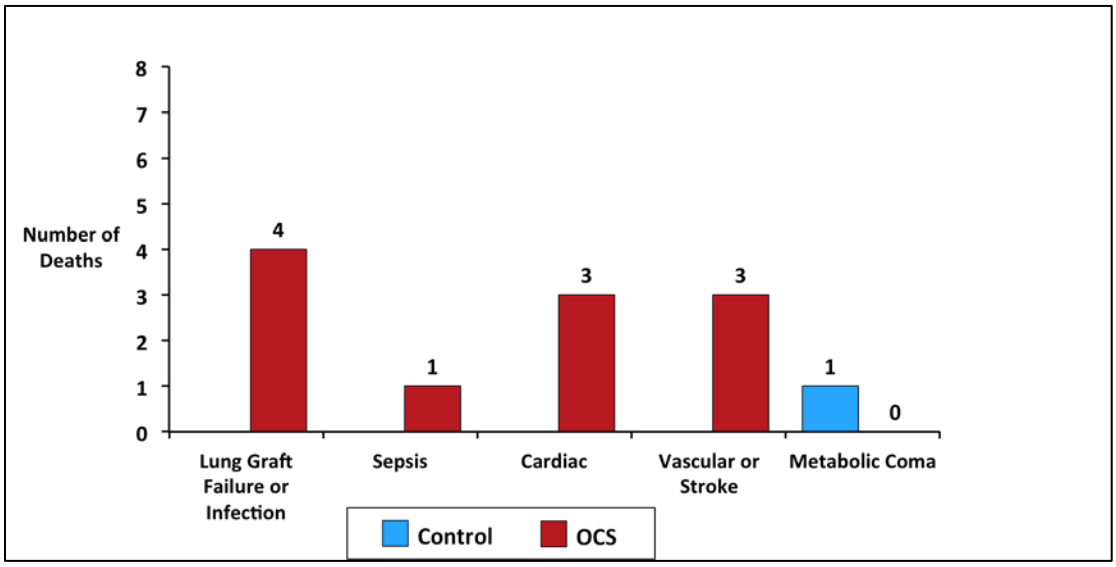


Figure 7: Causes of Death at 30 Days (ITT Population, Combined Cohort)

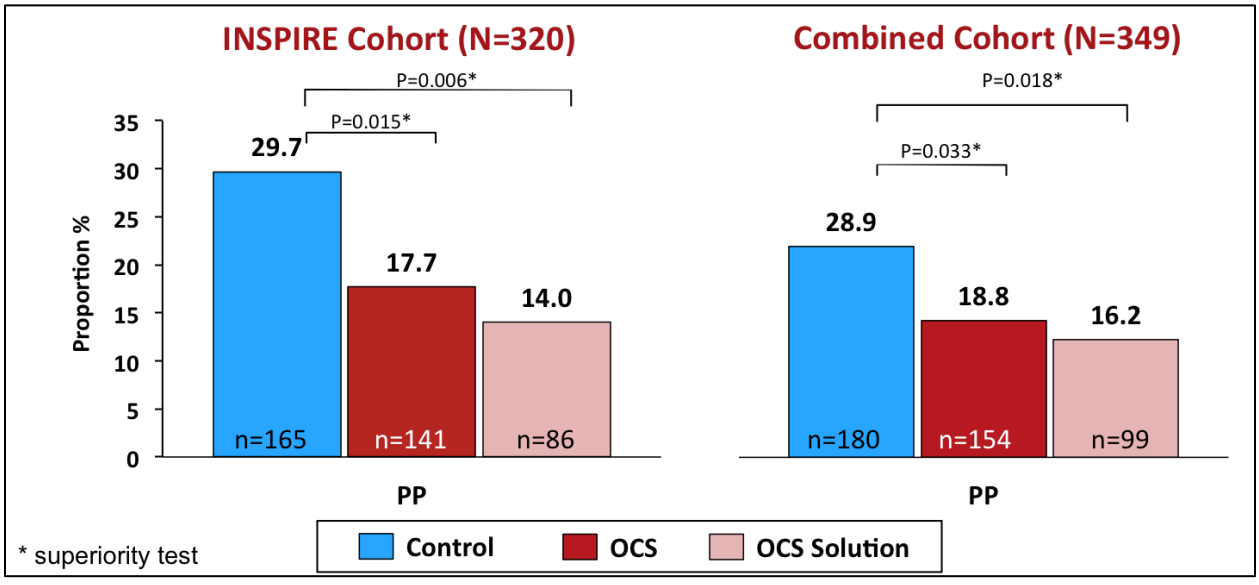


S. Incidence of PGD3 within 72 Hours

Figure 8 below provide the results for one of the components of the composite primary endpoint, i.e., of the incidence of PGD3 within the initial 72 hours post-transplantation. Results are shown for both the INSPIRE Cohort and the Combined Cohort, respectively.

In the Combined Cohort, the OCS arm and the OCS Solution subgroup were shown to be statistically superior in reducing PGD3 within the initial 72 hours as compared to the Control arm in the PP population (OCS arm p=0.033, OCS Solution subgroup p=0.018). In the PP population, the incidence of PGD3 was reduced by about a third for the overall OCS arm compared to Control, and by nearly half for OCS patients who were transplanted using OCS Lung Solution.

Figure 8: Incidence of PGD3 within 72 hours (p-values indicate superiority)



T. 30-Day and In-Hospital Survival

As previously shown, survival at Day 30 was lower in the OCS arm compared to control; however, survival at initial hospital discharge beyond Day 30 is similar in both arms. Mortality at Day 30 and at initial hospital discharge post-lung transplantation (if greater than 30 days) provides a more comprehensive assessment of early post-transplant mortality since some patients suffering from transplant-related complications may live past 30 days post-transplant, but die prior to discharge (i.e., surgical mortality). This analysis also provides another perspective on clinical benefit, since living through day 30, but dying in the hospital – with or without PGD3 – is clearly not a favorable patient outcome (see Figure 9 below).

There were 24 deaths in the INSPIRE study prior to Day 30 and prior to initial hospital discharge (12 Control and 12 OCS). Figure 10 below shows the adjudicated causes of deaths for the above 24 early mortalities who died at 30 days or In Hospital. There were more deaths in the Control arm from lung graft failure or infection as compared to OCS arm (8 vs 4) while there were more cardiac deaths in the OCS arm as compared to Control (4 vs 1).

This finding underscores the importance of assessing early mortality throughout the initial hospital discharge after transplantation to capture the full clinical picture for those patients who were suffering from transplant-related complications, that resulted in their mortality after the 30-day timepoint but before being discharged from the hospital.

Figure 9: 30-Day and In-Hospital Survival for OCS and Control Groups (INSPIRE Cohort and Combined cohort

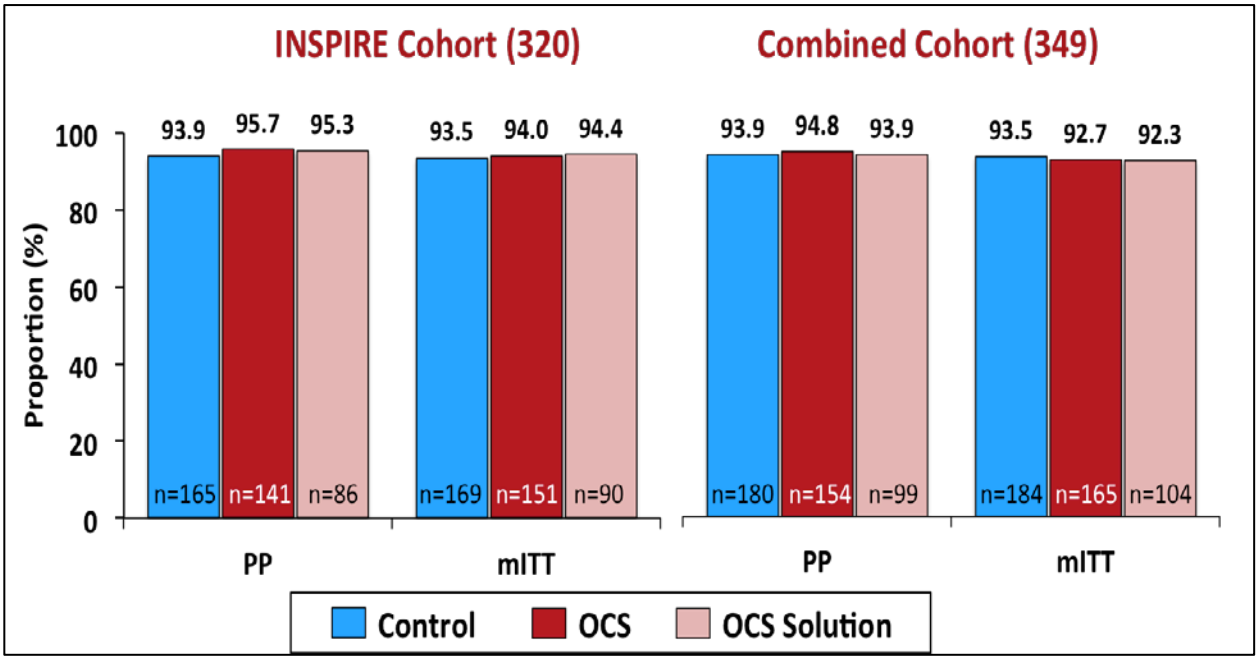
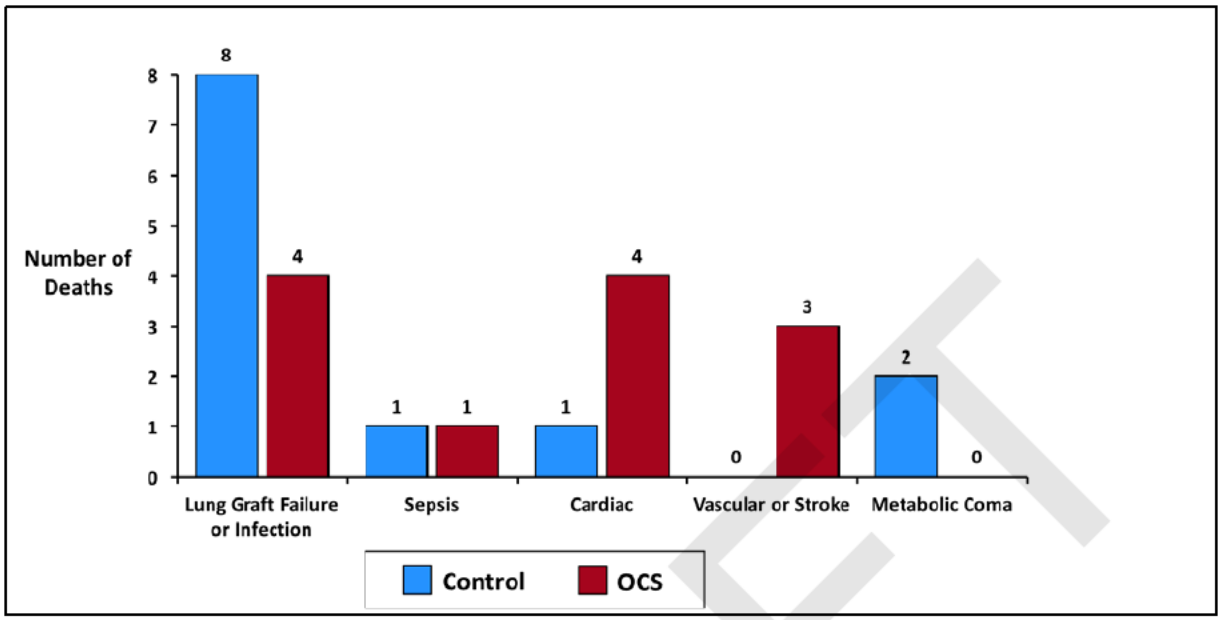


Figure 10: Summary Causes of Death for All 30-day and Initial In-Hospital Mortality Post-Lung Transplantation (Combined Cohort, mITT Population)



U. Secondary Effectiveness Endpoints

The results for the Secondary Endpoints are s own in Tab 0 below.

Table 10: Results for Second y Effectiven s ndpoints (PP Population)

Parameter	Contr (N=180	OCS Arm (N=154)	OCS Solution Subgroup (N=99)
Incidence of ISHLT PGD grade t 7 hours post-transplant ti n			
Proportion (π) (% (n/N)[1]	5.0% (9/179)	3.9% (6/154)	5.1% (5/99)
95% CI for P portion[2]	(2.3%, 9.3%)	(1.4%, 8.3%)	(1.7%, 11.4%)
πocs - πControl ( ) (one-sided 95% I)[3]		-1.1% (-∞, 2.6%)	0.0% (-∞, 4.5%)
p-value of non-Inferi ty test[4]		0.0033	0.0347
Incidence of ISHLT PG gr de 2 or 3 at 72 hours post-transplantat on			
Proportion (π) (%) (n/N)[1]	10.6% (19/179)	13.0% (20/154)	10.1% (10/99)
95% CI for Proportion[2]	(6.5%, 16.1%)	(8.1%, 19.3%)	(5.0%, 17.8%)
πocs - πControl (%) (one-sided 95% CI)[3]		2.4% (-∞, 8.2%)	-0.5% (-∞, 5.7%)
p-value of non-Inferiority test[4]		0.0746	0.0176
Patient survival at day 30 post-transplantation			
Proportion (π) (%) (n/N)[1]	100.0% (180/180)	94.8% (146/154)	93.9% (93/99)

Parameter	Control (N=180)	OCS Arm (N=154)	OCS Solution Subgroup (N=99)
95% CI for Proportion[2]	(98.0%, 100.0%)	(90.0%, 97.7%)	(87.3%, 97.7%)
πControl - πocs (%) (one-sided 95% CI)[3]		5.2% (-∞, 8.1%)	6.1% (-∞, 10.0%)
p-value of non-Inferiority test[4]		--	0.8049

V. Other Clinical Endpoints

The results for the Other Clinical Endpoints specified in the protocol shown in Table 11 for the PP a population. These analyses provide supporting evidence r the fectiveness of the OCS Lung System in reducing the incidence of PGD following lung transpla tion.

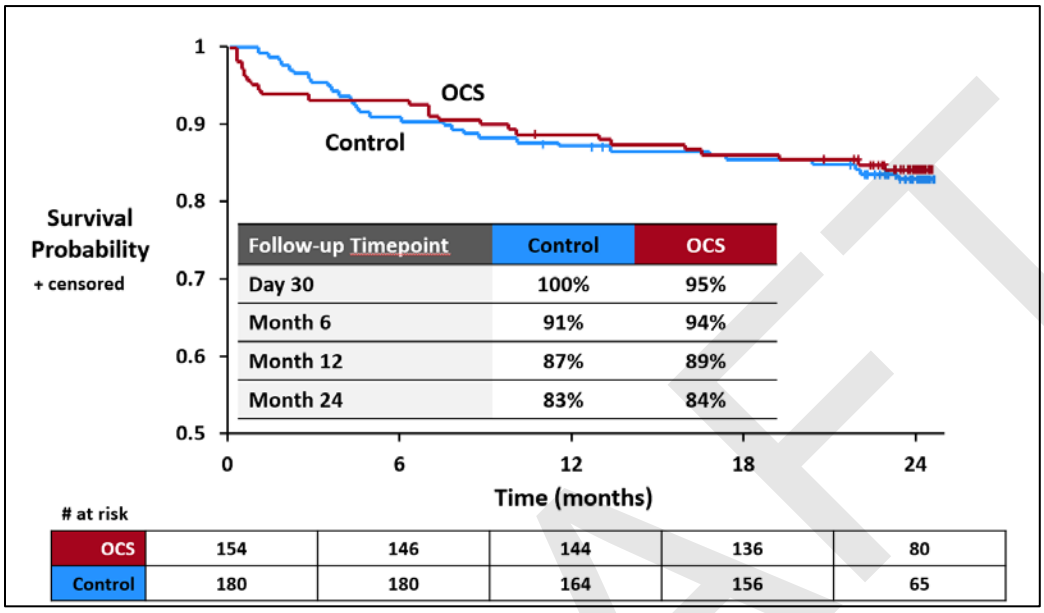
Table 11: Results for Other Effectiveness Endpoints, P Population, Combine Cohort

Parameter	Control (N=180)	OCS A m (N= 4)	OCS Solution Subgroup (N=99)
Incidence of ISHLT PGD grade 3 in the first 72 hours			
Proportion (π) (%) (n/N)[1]	28.9% (52 80)	18.8% (/154)	16.2% (16/99)
95% CI for Proportion[2]	(22.4%, 36. %)	(0% 25.9%)	(9.5%, 24.9%)
p-value of superiority test[3]		0.0325	0.0178
Incidence of ISHLT PGD g de 2 or n the firs 72 hours			
Proportion (π) (%) (n/N)[1]	60.6 (109/180)	44.2% (68/154)	44.4% (44/99)
95% CI for Proportion[2]	.0%,	(36.2%, 52.4%)	(34.5%, 54.8%)
p-value of superiority test[3]		0.0028	0.0097
Survival at itial hosp l discha e			
Proporti n (π) (%) (n/N)[1]	93.9% (169/180)	96.1% (148/154)	94.9% (94/99)
95% CI fo Proportion[2]	(89.3%, 96.9%)	(91.7%, 98.6%)	(88.6%, 98.3%)
p-value of sup ority test[3]		0.3586	0.7154
Survival at day 3 nd sence of ISHLT PGD grade 2 or 3 in the first 72 hours			
Proportion (π) (%) (n/N)[1]	39.4% (71/180)	54.5% (84/154)	54.5% (54/99)
95% CI for Proportion[2]	(32.3%, 47.0%)	(46.3%, 62.6%)	(44.2%, 64.6%)
p-value of superiority test[3]		0.0058	0.0152
Survival at day 30 and hospital discharge and absence of ISHLT PGD grade 2 or 3 in the first 72 hours			
Proportion (π) (%) (n/N)[1]	38.3% (69/180)	54.5% (84/154)	54.5% (54/99)
95% CI for Proportion[2]	(31.2%, 45.9%)	(46.3%, 62.6%)	(44.2%, 64.6%)
p-value of superiority test[3]		0.0030	0.0091

W. Survival Analyses through 24 Months

The INSPIRE study is designed with a total of 24 months of follow-up for all subjects. All survival data are illustrated graphically in Figure 11 for the PP population. At 12 and 24 months, the survival rates are similar for the OCS Arm and Control.

Figure 11: K-M Survival for OCS and Control groups at 24 Months (Combined Cohort, PP Population)

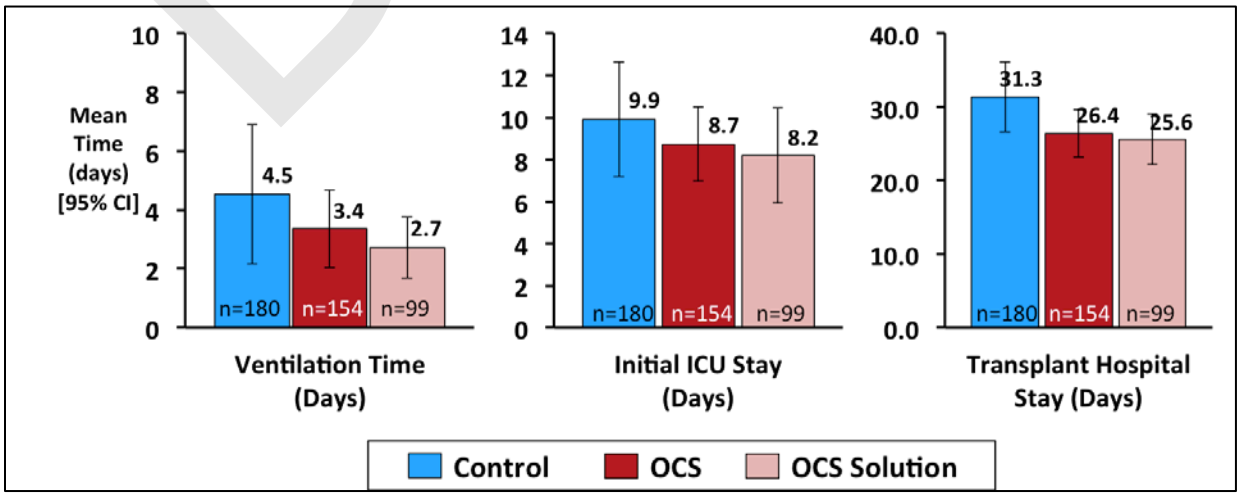


Follow-up Timepoint	Control	OCS
Day 30	100%	95%
Month 6	91%	94%
Month 12	87%	89%
Month 24	83%	84%

X. Additional Analyses

The duration of initial p st-transplan ventilation, t e length of initial post-transplant ICU time and length of initial post- nspla hospital s y are shown in Figure 12 below. The results show a numerical improvem for the OCS arm and OCS Lung Solution subgroup as compared to the Control se resul are relevant given the clinical and economic benefits that result from a redu ion in venti ion supp rt time, ICU, and hospital stay.

Figure 1 Ventilator Su ort, Initial ICU Time, and Initial Hospital Stay for OCS and Control Grou (PP Population)



Y. Primary Safety Endpoint

The INSPIRE Trial met its primary safety endpoint defined as the average number of lung graft-related serious adverse events up to 30 days follow-up after lung transplantation, consisting of the following SAEs (at least one per type): acute rejection (biopsy proven); respiratory failure; bronchial anastomotic complications; and major pulmonary-related infection. Table 12 and Table 13 below show the results of the primary safety analysis for the INSPIRE Trial in the INSPIRE and Combined Cohorts Safety Populations.

Table 12: Primary Safety Endpoint Analysis – (Average Number of Lung Graft-Related SAEs) in INSPIRE Cohort Safety Population

	Safety & T Population		
Number of lung graft-related serious adverse events up to the 30-day follow-up after transplantation (at most one per type)[1]	**Control (N= 169)**	**OC Arm (N=1)**	**OCS Solution (N=89)**
Mean ± SD	0.28 ± 0.53	0.23 ± 0.45	0.26 ± 0.49
Median	0 0	0.0	0.0
Min.-Max.	0.0 - 2	0.0 - 2.0	0.0 - 2.0
95% Confidence Interval of mean	(0.20, 0.36)	(0.16, 0.31)	(0.16, 0.36)
Difference in mean (one-sided 95% CI)		0.045 (-∞, 0.047)	-0.020 (-∞, 0.093)
p-value of non-inferiority test[2]		0.0195	0.0942
p-value of two-sample t-test[3]		0.4195	--

[1] Multiple occurrences of the same of events o ne patient are counted once only.
[2] p-value of non-inferiority test i ased on -sided tw ample t-test with a non-inferiority margin of 0.07.
[3] p-value of superiority test is sed on two- ded two-sam t-test for a difference in means between treatment groups. The test for superiority wil e performed ly if non-inferi ty has been demonstrated.

Table 13: Primary Sa y En point Analys – (Average Number of Lung Graft-Related SAEs) in Com ed Cohort Safety Population

	Safety & AT Population		
Numbe of lung graft-related AEs up to the 30-day after nsplantation (at m t one per type)[1]	**Control (N=184)**	**OCS Arm (N=164)**	**OCS Solution (N=103)**
Mean ± SD	0.29 ± 0.54	0.26 ± 0.48	0.30 ± 0.52
Median	0.0	0.0	0.0
Minimum - Maximum	0.0 - 2.0	0.0 - 2.0	0.0 - 2.0
95% CI for Mean	(0.21, 0.37)	(0.19, 0.34)	(0.20, 0.40)
Difference in mean (one-sided 95% CI)		-0.026 (-∞, 0.065)	0.013 (-∞, 0.121)
p-value of non-inferiority test[2]		0.0417	0.1931
p-value of two-sample t-test[3]		0.6400	--

[1] Multiple occurrences of the same category of events on one patient are counted once only.
[2] p-value of non-inferiority test is based on one-sided two-sample t-test with a non-inferiority margin of 0.07.
[3] p-value of superiority test is based on two-sided two-sample t-test for a difference in means between treatment groups. The test for superiority will be performed only if non-inferiority has been demonstrated.

Z. Incidence of Lung Graft-Related Serious Adverse Events during First 30 Days Post-Transplantation

The events that comprise the primary safety endpoint are described in more detail in Table 14 and Table 15 below, for the INSPIRE and Combined Cohorts, respectively. The incidence of LGRSAEs was similar in both group the OCS and Control groups.

Table 14: Number of LGRSAEs during First 30 Days Post-Transplant, Safety Population (INSPIRE Cohort)

Parameter	Safety Population (INSPIRE Cohort)					
	Control		OCS Arm		OCS Solution	
	Patients (n=169)	Events (n=48)	Patients (n=150)	E ts n=3	Patients (n=89)	Events (n=25)
Lung graft-related serious adverse events - 30 days	40 (23.7%)	48 (100%)	33 (22.0%)	37 (100%)	21 (23.6%)	25 (100%)
Acute Rejection[1]	4 (2.4%)	4 (8.3%)	2 1.3%)	(5.4%)	2 (2.2%)	2 (8.0%)
Respiratory Failure[2]	14 (8.3%)	14 (29.2%)	19 (1 7%)	20(54.1%)	11(12.4%)	12 (48.0%)
Bronchial Anastomotic Complications	4 (2.4%)	4 (8.3%)	0 (0.0%	0 (0.0%)	0 (0.0%)	0 (0.0%)
Major Pulmonary-Related Infection	25 (14.8%)	26 (54 %)	9 3%)	1 (40.5%)	10 (11.2%)	11 (44.0%)

[1] Biopsy proven moderate to severe according to the ISHL wor ng formulation of pathology grading
[2] Impairment of respiratory function re ng intubation, cheostomy or the inability to discontinue invasive ventilatory support within 4 days (96 hours) pos ransplant

Table 15: Number of GRS Es during F 30 Days Post-Transplant, Safety Population (Combined Co t)

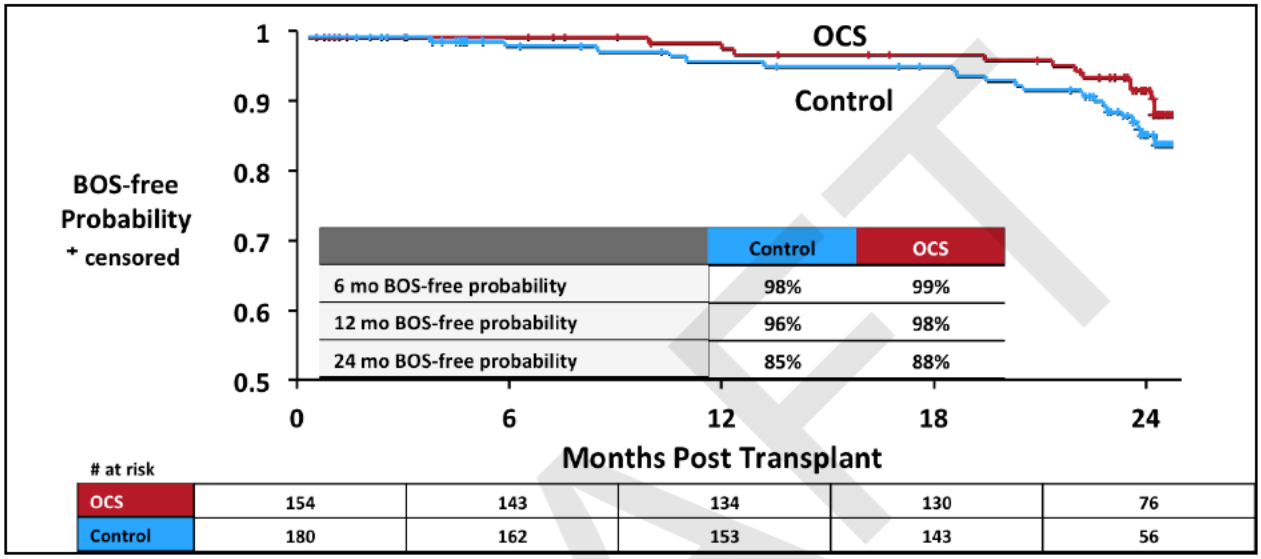
Parameter	Control		OCS Arm		OCS Solution	
	atients =184)	Events (N=55)	Patients (N=164)	Events (N=45)	Patients (N=103)	Events (N=33)
Lung graft-related s us adverse events up to th 30-day follow-up after transplant n[1]	4 (24.5%)	55 (100.0%)	40 (24.4%)	45 (100.0%)	28 (27.2%)	33 (100.0%)
Acute Rejection[2]	4 (2.2%)	4 (7.3%)	2 (1.2%)	2 (4.4%)	2 (1.9%)	2 (6.1%)
Respiratory Failure[3]	16 (8.7%)	16 (29.1%)	23 (14.0%)	24 (53.3%)	15 (14.6%)	16 (48.5%)
Bronchial Anastomotic Complication	4 (2.2%)	4 (7.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Major Pulmonary-Related Infection	29 (15.8%)	31 (56.4%)	18 (11.0%)	19 (42.2%)	14 (13.6%)	15 (45.5%)

[1] Biopsy proven moderate to severe according to the ISHLT working formulation of pathology grading
[2] Impairment of respiratory function requiring re-intubation, tracheostomy or the inability to discontinue invasive ventilatory support within 4 days (96 hours) post-transplant.

AA. Incidence of BOS through 24 Months

BOS is the most common long-term complication after lung transplantation and is the leading cause of long-term graft failure in lung transplantation. Figure 13 below demonstrates the results of the overall 24-month KM freedom from BOS analysis. The OCS arm showed a numerically higher percentage of patients who were free from BOS as compared to the Control arm at 24 months (88% for OCS compared to 85% for the control group).

Figure 13: Overall 24 Month BOS-Free Probability Analysis (Combined Cohort, PP)



BB. Summary of Adver Event

Table 16 below shows th Adverse E ents by type at were observed in the INSPIRE trial. The frequency of adverse ev s was si n the Control and OCS groups.

Table 16: Adverse Even y Type (Safety Population, Combined Cohort)

Parameter	Control (N=184)	OCS Arm (N=164)	OCS Solution (N=103)
Patients w Any Type of Adv se Events	152 (82.6%)	136 (82.9%)	86 (83.5%)
Patients with A verse Events efinitely Related to OCS o Control	0 (0.0%)	0 (0.0%)	0 (0.0%)
Patients with Adverse nts Probably Related to OCS or Control	0 (0.0%)	1 (0.6%)	1 (1.0%)
Patients with Adverse Events Possibly Related to OCS or Control	5 (2.7%)	5 (3.0%)	2 (1.9%)
Patients with Adverse Events Unlikely Related to OCS or Control	57 (31.0%)	59 (36.0%)	35 (34.0%)
Patients with Adverse Events Unrelated to OCS or Control	131 (71.2%)	113 (68.9%)	70 (68.0%)
Patients with Adverse Events Unanticipated	0 (0.0%)	0 (0.0%)	0 (0.0%)

Parameter	Control (N=184)	OCS Arm (N=164)	OCS Solution (N=103)
Patients with Any Serious Adverse Events	116 (63.0%)	92 (56.1%)	58 (56.3%)
Patients with Any Severe Adverse Events	54 (29.3%)	51 (31.1%)	31 (30.1%)
Deaths up to 24 months[1]	31 (16.8%)	28 (17.1%)	19 (18.4%)

OCS arm death count includes Subject (b) (6) who was withdrawn from study first, then followed by re-transplantation and died afterwards.
All Adverse Events were up to 30 days post-transplantation or initial hospital discharge, LGR SAEs were up to 6 months post-transplantation.

Table 17 below presents the Adjudicated SAEs that were observed i ≥ % of patients in the Control and OCS arms.

Table 17: Adjudicated SAEs by System Organ Class and Preferred Term that occurred in ≥ 1% of Patients, Safety Population

System Organ Class and Preferred Term		Control n (%)		OCS Arm (%)		OCS Solution n (%)	
		Patients (N=184)	Events (N=247)	Patients (N=164)	Events (N=192)	Patients (N=103)	Events (N=118)
Total		**116 (63.0)**	**247 (100.0)**	**92 (56)**	**192 (100.0)**	**58 (56.3)**	**118 (100.0)**
Respiratory, thoracic and mediastinal disorders		**57 (31.0)**	**74 (30.0)**	**47 (28.7)**	**(30.7)**	**29 (28.2)**	**37 (31.4)**
	Respiratory failure	17 (9.2)	18 (7.3)	20 (12.2)	22 (11.5)	13 (12.6)	15 (12.7)
	Pleural effusion	12 (6.5)	12 (4.9)	6 ( )	7 (3.6)	3 (2.9)	4 (3.4)
	Pneumothorax	12 (6.5)	12 (4.9)	(3.0)	6 (3.1)	3 (2.9)	4 (3.4)
	Haemothorax	9 (4.9)	(6)	7 (3)	8 (4.2)	2 (1.9)	3 (2.5)
	Bronchostenosis	4 (2.2)	5 2.0)	5 (3.0)	5 (2.6)	3 (2.9)	3 (2.5)
	Pulmonary embolism	4 (2.2)	4 (6)	3 1.8)	3 (1.6)	2 (1.9)	2 (1.7)
	Bronchial disorder	3 (1	4 (1.	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Bronchial secretion retention	2 (1.1)	2 (0.8)	2 (1.2)	2 (1.0)	0 (0.0)	0 (0.0)
	Acute respiratory failure	1 (0.5)	1 (0 4)	2 (1.2)	2 (1.0)	2 (1.9)	2 (1.7)
	Chylothorax	2 1)	2 (0.8)	1 (0.6)	1 (0.5)	1 (1.0)	1 (0.8)
	Bronchopleural fistula	2 (1.1	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations		**5 (30.4)**	**72 (29.1)**	**38 (23.2)**	**43 (22.4)**	**26 (25.2)**	**29 (24.6)**
	Pneumonia	20 (.9)	20 (8.1)	14 (8.5)	15 (7.8)	10 (9.7)	11 (9.3)
	Lung infection	7 (8)	8 (3.2)	3 (1.8)	3 (1.6)	2 (1.9)	2 (1.7)
	Bronchopneumonia	(1.6)	3 (1.2)	5 (3.0)	5 (2.6)	3 (2.9)	3 (2.5)
	Infection	5 (2.7)	5 (2.0)	3 (1.8)	3 (1.6)	1 (1.0)	1 (0.8)
	Bronchitis	4 (2.2)	4 (1.6)	1 (0.6)	1 (0.5)	0 (0.0)	0 (0.0)
	Bronchopulmonary aspergillosis	4 (2.2)	4 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

System Organ Class and Preferred Term		Control n (%)		OCS Arm n (%)		OCS Solution n (%)	
		Patients (N=184)	Events (N=247)	Patients (N=164)	Events (N=192)	Patients (N=103)	Events (N=118)
	Lung infection pseudomonal	1 (0.5)	1 (0.4)	3 (1.8)	3 (1.6)	2 (1.9)	2 (1.7)
	Respiratory tract infection	2 (1.1)	2 (0.8)	2 (1.2)	2 (1.0)	2 (1.9)	2 (1.7)
	Sepsis	4 (2.2)	4 (1.6)	0 (0 0	0 (0.0)	0 (0.0)	0 (0.0)
	Staphylococcal infection	3 (1.6)	3 (1.2)	1 (0.6)	(0.5)	1 (1.0)	1 (0.8)
	Wound infection	4 (2.2)	4 (1.6)	0 (0.0)	0 ( )	0 (0.0)	0 (0.0)
	Diverticulitis	2 (1.1)	2 (0.8)	1 (0.6)	1 (0.5)	1 (1.0)	1 (0.8)
	Aspergillosis	0 (0.0)	0 (0.0)	2 2)	2 (1.0)	1 (1.0)	1 (0.8)
	Clostridium difficile colitis	2 (1.1)	2 (0.8)	(0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Cytomegalovirus infection	2 (1.1)	(0	0 (0	0 (0.0)	0 (0.0)	0 (0.0)
	Pseudomonas infection	0 (0.0)	0 .0)	2 (1.2)	2 (1.0)	2 (1.9)	2 (1.7)
	Septic shock	2 (1.1)	2 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders		**16 (7)**	**17 (6.**	**15 (9.1)**	**20 (10.4)**	**11 (10.7)**	**13 (11.0)**
	Atrial fibrillation	(3.3)	7 (2.8)	7 (4.3)	7 (3.6)	5 (4.9)	5 (4.2)
	Cardiac arrest	(0.0)	0 0)	5 (3.0)	6 (3.1)	4 (3.9)	4 (3.4)
	Arrhythmia	2 (	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Atrial flutter	2 (1.1)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Cardiac failure con tive	0 0.0)	0 (0.0)	2 (1.2)	2 (1.0)	1 (1.0)	1 (0.8)
	Cardiac tamponade	2 ( )	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders		**13 .1)**	**13 (5.3)**	**13 (7.9)**	**13 (6.8)**	**7 (6.8)**	**7 (5.9)**
	Renal failure acute	(3.3)	6 (2.4)	11 (6.7)	11 (5.7)	7 (6.8)	7 (5.9)
	Renal failure	7 (3.8)	7 (2.8)	2 (1.2)	2 (1.0)	0 (0.0)	0 (0.0)
Vascular disorders		**9 (4.9)**	**10 (4.0)**	**11 (6.7)**	**14 (7.3)**	**6 (5.8)**	**7 (5.9)**
	Haemorrhage	5 (2.7)	5 (2.0)	5 (3.0)	5 (2.6)	3 (2.9)	3 (2.5)

System Organ Class and Preferred Term		Control n (%)		OCS Arm n (%)		OCS Solution n (%)	
		Patients (N=184)	Events (N=247)	Patients (N=164)	Events (N=192)	Patients (N=103)	Events (N=118)
	Deep vein thrombosis	1 (0.5)	1 (0.4)	4 (2.4)	4 (2.1)	2 (1.9)	2 (1.7)
	Ischaemia	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.0)	1 (1.0)	1 (0.8)
Injury, poisoning and procedural complications		**10 (5.4)**	**10 (4.0)**	**11 (6**	**11 (5.7)**	**7 (6.8)**	**7 (5.9)**
	Post procedural haemorrhage	1 (0.5)	1 (0.4)	6 (3.7)	6 1)	3 (2.9)	3 (2.5)
	Wound dehiscence	2 (1.1)	2 (0.8)	3 (1.8)	3 (1.6)	3 (2.9)	3 (2.5)
	Procedural complication	2 (1.1)	2 (0.8)	1 (0)	1 (0.5)	0 (0.0)	0 (0.0)
Gastrointestinal disorders		**13 (7.1)**	**17 (6.9)**	**(1.2)**	**2 (1.0)**	**1 (1.0)**	**1 (0.8)**
	Impaired gastric emptying	2 (1.1)	8)	1 6)	1 (0.5)	1 (1.0)	1 (0.8)
	Diarrhoea	2 (1.1)	2 0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Gastrointestinal haemorrhage	2 (1.1)	2 (8)	0 .0)	0 (0.0)	0 (0.0)	0 (0.0)
	Large intestine perforation	2 (1 1	2 (0.	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders		**1 (6.5)**	**12 (4.9**	**6 (3.7)**	**6 (3.1)**	**5 (4.9)**	**5 (4.2)**
	Lung transplant rejection	12 (6.5)	12 (4.9)	5 (3.0)	5 (2.6)	4 (3.9)	4 (3.4)
Nervous system disorders		**8 3)**	**8 (3.2)**	**8 (4.9)**	**9 (4.7)**	**4 (3.9)**	**4 (3.4)**
	Cerebrovascular accident	0 (0.0	0 (0.0)	4 (2.4)	4 (2.1)	1 (1.0)	1 (0.8)
	Encephalopathy	(1.1)	2 (0.8)	1 (0.6)	1 (0.5)	0 (0.0)	0 (0.0)
	Brain oedema	2 (1)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Convulsion	2 (1)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions		**(2.7)**	**5 (2.0)**	**3 (1.8)**	**3 (1.6)**	**3 (2.9)**	**3 (2.5)**
Blood and lymphatic system disorders		**1 (0.5)**	**1 (0.4)**	**3 (1.8)**	**3 (1.6)**	**1 (1.0)**	**1 (0.8)**
Psychiatric disorders		**4 (2.2)**	**4 (1.6)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
	Delirium	2 (1.1)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

System Organ Class and Preferred Term	Control n (%)		OCS Arm n (%)		OCS Solution n (%)	
	Patients (N=184)	Events (N=247)	Patients (N=164)	Events (N=192)	Patients (N=103)	Events (N=118)
Metabolism and nutrition disorders	2 (1.1)	2 (0.8)	1 (0.6)	1 (0.5)	1 (1.0)	1 (0.8)
Musculoskeletal and connective tissue disorders	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.0)	1 (1.0)	1 (0.8)
Surgical and medical procedures	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.0)	1 (1.0)	1 (0.8)

CC. Summary of INSPIRE Clinical Study

The INSPIRE Trial is a randomized, controlled, multi-center study at 21 investigational sites in the U.S., Canada, Australia, and the European Union.

The primary effectiveness objective was met in this study and the OCS Lung System was shown to be statistically non-inferior to the standard of care cold storage in the PP Population (the primary analysis population). The treatment differences in the OCS Solution subgroup, which reflects the results with the to-be-commercialized product, demonstrated even more favorable results compared to Control. Analyses of the mITT population indicate that the non-inferiority statistical test was not met, but the difference is still in favor of the OCS arm

Patients who received donor lungs preserved with the OCS Lung Syste had a significantly lower incidence of PGD3 within 72 hours.

The OCS arm and OCS Solution subgroup successfully met the s fety endp t that was defined as the average number of LGRSAEs up to the 30-day follow p after transplan tion, consisting of the following serious adverse events:

- Acute rejection (biopsy proven)
- Respiratory failure
- Bronchial anastomotic complication
- Major pulmonary-related infect n.

The OCS arm and the OCS Solution subgrou success lly t the non-inferiority test for the safety endpoint above in the Safety population naly is as compared to Control arm $p<0.0001$. The assessment of all SAEs, lu g g ft-related Es, and AEs did not demonstrate any safety concerns.

Numerical improvemen were obser d in the OC arm for initial post-transplant mechanical ventilation time, initial I U stay, l g f i itial post-transplant hospital stay as compared to the Control arm. These r ul are relevant given the clinical and economic benefits that result from a reduction ntilation pport time, ICU, and hospital stay.

Assessmen of BOS is on ing for to 24 months. To date, the data show a numerically lower incidenc of BOS at the 24 onth follow-up for the OCS arm as compared to the control. BOS is a chronic ndition that deve ps between 2 and 5 years following lung transplantation. The sponsor plan to evaluate thi trend for an additional 3 years (up to 5 years post-transplant) in a proposed post-m rket stud

Finally, it is import t note that these benefits in clinical outcomes were obtained even though the out of body time was significantly longer than the control. The OCS technology allows for a reduction in total ischemic time for the donor lung graft as compared to standard of care, while increasing the out-of-body time.

In summary, the INSPIRE Trial was a, multi-center, randomized controlled international trial of the OCS Lung System compared to the standard of care. The results of this trial of 349 patients provide strong evidence for the safety and effectiveness of the OCS Lung System for the proposed indication for use (i.e., preservation of standard criteria donor lungs).

XI. SUMMARY OF OTHER CLINICAL INFORMATION – EUROPEAN PILOT STUDY

Prior to initiating the INSPIRE study, TransMedics conducted European pilot studies of the OCS Lung System. These cases were conducted in two leading lung transplant centers in Germany (Hannover Medical School (MHH) in Hannover, Germany) and Spain (University Puerta de Hierro Majdahonda Hospital in Madrid Spain). Both institutions received local ethics committee approval for the use of OCS on their patients in this program.

Between February and July 2011, a total of 13 double lung transplant procedures were performed after the lungs were preserved on the OCS Lung System.

These clinical cases followed the current standard acceptance criteria f donors in the participating centers. There were no exclusion criteria for recipients . all active waiting list patients at the participating centers were considered once an appr priate d or match was identified.

Data are available on the following endpoints: 30-day pati nt and graft survival, idence of PGD3 at 72 hours.

A. Donor Demographics

Donor demographics including significant risk factors, incl ng:

- 1 donor was a donor from unco ro d Type 1 DCD nor with 118 minutes of warm ischemia + 285 minutes of cold i hemia f re the use f OCS Lung System
- 4 donors had abnormal chest x-ray nd hi ory of p eumonia
- 1 donor was 72 ye old

Recipients also presented cipient ris factors fo rimary graft dysfunction after lung transplantation includi

- 6 patients with p ima diagnosis of Idiopathic Pulmonary Fibrosis
- 2 p ith Prim y Pulmonary Hypertension
- patients wer n ECM support prior to transplantation on the high-urgent waiting list

B. Clinical utcomes and urvival

Clinical outcome includ g survival, for the 13 patients is shown in Table 18 below. There were 2 patients that rienced PGD3, one at T0 and one at T48. These incidences were due to severe recipient lung infection at the time of transplantation and for acute rejection, respectively. In both cases the patients fully recovered and were discharged with good lung function. All patients (100%) survived 30 days post-transplantation. In addition, the post-transplant transbronchial biopsy showed no evidence of rejection or severe inflammation and healthy lung tissue.

Table 18: Post-Transplant Clinical Outcomes and Survival Results for 13 Subjects in European Pilot Study

Post-Transplant Outcomes	OCS Lung Results
ICU Time (days)	
Mean ± SD	12 ± 11
Median	6.1
Range	1.2 -31
Mechanical Ventilation Time (days)	
Mean ± SD	2.5 ± 5.1
Median	0.8
Range	0.4 - 9
Survival at 30-Day	
Patient [n (%)]	13 (100%)
Graft [n (%)]	(100)
Primary Graft Dysfunction (PGD) Grade 3	
T-72 [n (%)]	0/13 (0%
T-48 [n (%)]	13 (8%)
T-24 [n (%)]	0/13 (0%)
T-0 [n (%)]	1/13 (8%)

C. Summary of Adverse ven

There were 9 SAE ported f four patients including: (1) moderate pulmonary bleeding and (2) respirato failure, te rejec n post-discharge, moderate myocardial infarction, venous thromboe bolism, hemoth rax seco dary to chest tube placement and anti-coagulation therapy post-tra plant, pulmonary s psis and thrombocytopenia.

The early E pean clinical perience supports the safety and effectiveness of the OCS Lung System. The d show 10 % 30-day survival with no cases of organ loss. All lungs preserved on OCS were suc sful transplanted.

XII. PANEL RECOMMENDDATION

TBD

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

Preclinical data, including bench testing, biocompatibility testing, sterilization and shelf life, electrical safety and EMC, software validation and verification testing and animal testing demonstrate that the OCS Lung performs as intended and is safe for clinical use.

The OCS Arm and OCS Lung Solution subgroup successfully met the primary safety endpoint (i.e., the average number of lung graft-related serious adverse events up to the 30-day follow-up after transplantation), demonstrating non-inferiority test as compared to C ntrol Arm. The SAEs and Lung Graft-Related SAEs and AEs observed in the INSPIRE stud re those that are expected for lung transplantation and no safety signals were observ d. L g-term up to 24 months follow-up of patient survival is showing comparable tren s between he INSPIRE Trial groups.

B. Effectiveness Conclusions

The INSPIRE Trial was a prospective, multi-center, r domized ntrolled trial to evaluate the effect of the OCS Lung System on short and long term l g tr splant clinical outcomes in standard criteria lung transplantation compared to cold stor standard of care preservation.

The primary effectiveness objective was m i his study and th OCS Lung System was shown to be statistically non-inferior to the standar of care ld storage i the PP Population (the primary analysis population). The treatment fferenc in OCS Solution subgroup, which reflects the results with the commercialized pr duc demonstrated even more favorable results compared to Control. Analys of mITT po lation indicate that the non-inferiority statistical test was not met but the dif rence is s l in favor of the OCS arm.

Numerical improvemen were obse ed in the OC arm for initial post-transplant mechanical ventilation time, initial ICU stay d lengt itial post-transplant hospital stay as compared to the Control arm. These r s are relevant given the clinical and economic benefits that result from a reducti tilation pport time, ICU, and hospital stay.

Assessmen of BOS is ong ing for to 24 months. To date, the data show a numerically lower inciden of BOS at the 24 onth follow-up for the OCS arm as compared to the control. BOS is a chron condition that de elops between 2 and 5 years following lung transplantation. The sponsor plan o evaluate th trend for an additional 3 years (up to 5 years post-transplant) in a proposed post-m rket stud

C. Overall Benefit-Risk Conclusions

The preclinical and clinical data presented in this PMA application support the safety and effectiveness of the OCS Lung System for the proposed intended use, i.e., preservation of donor lungs in a near physiologic, ventilated and perfused state for subsequent transplantation into a recipient. The results demonstrate that the OCS Lung System provides similar or superior clinical results to the standard of care cold storage solution while allowing for extended cross clamp time and the ability to monitor the conditions of the donor lungs. Technologies, such as the OCS Lung System, have the ability to improve outcomes for patients undergoing lung transplantation. These benefits outweigh the risks.

XIV. CDRH DECISION

The final conditions of approval cited in the approval order are described below:

- COA 1
- Etc.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

CDRH issued an approval order on [date].

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See ap oval order