OCS™ Heart System for the Resuscitation, Preservation, and Assessment of Donor Hearts

April 6, 2021

Circulatory System Devices Panel

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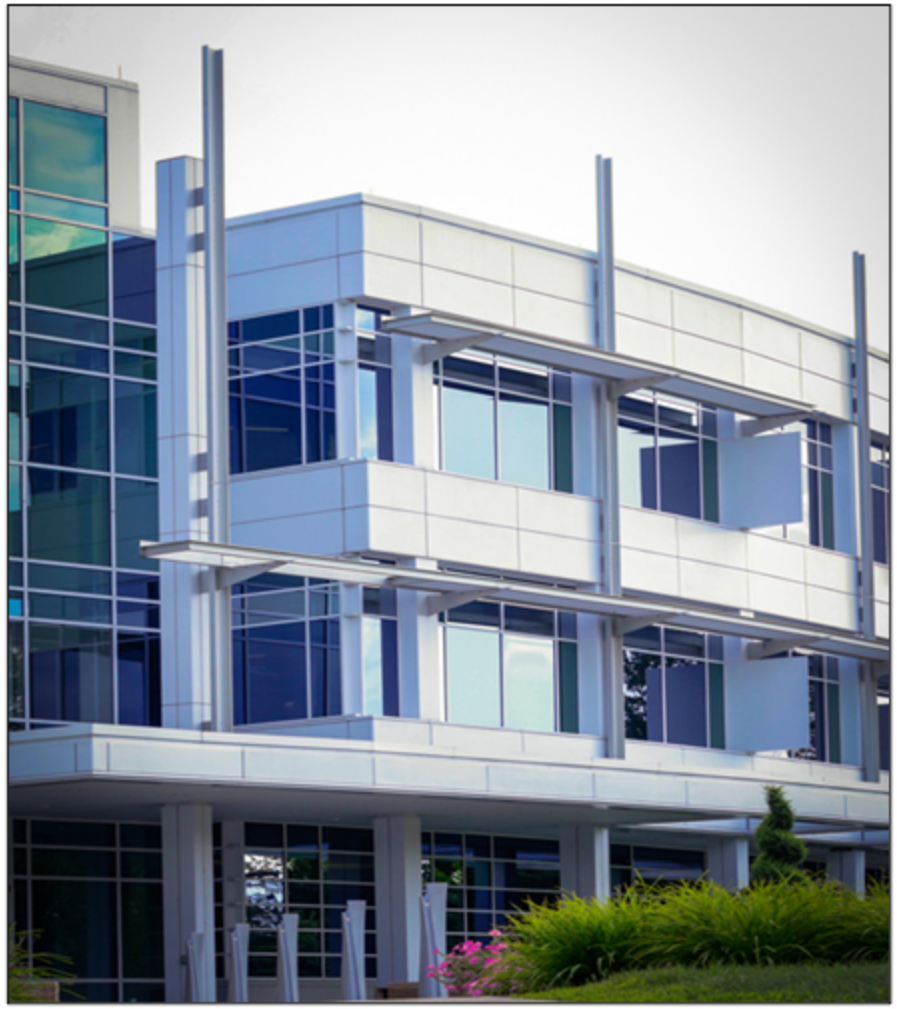
Introduction

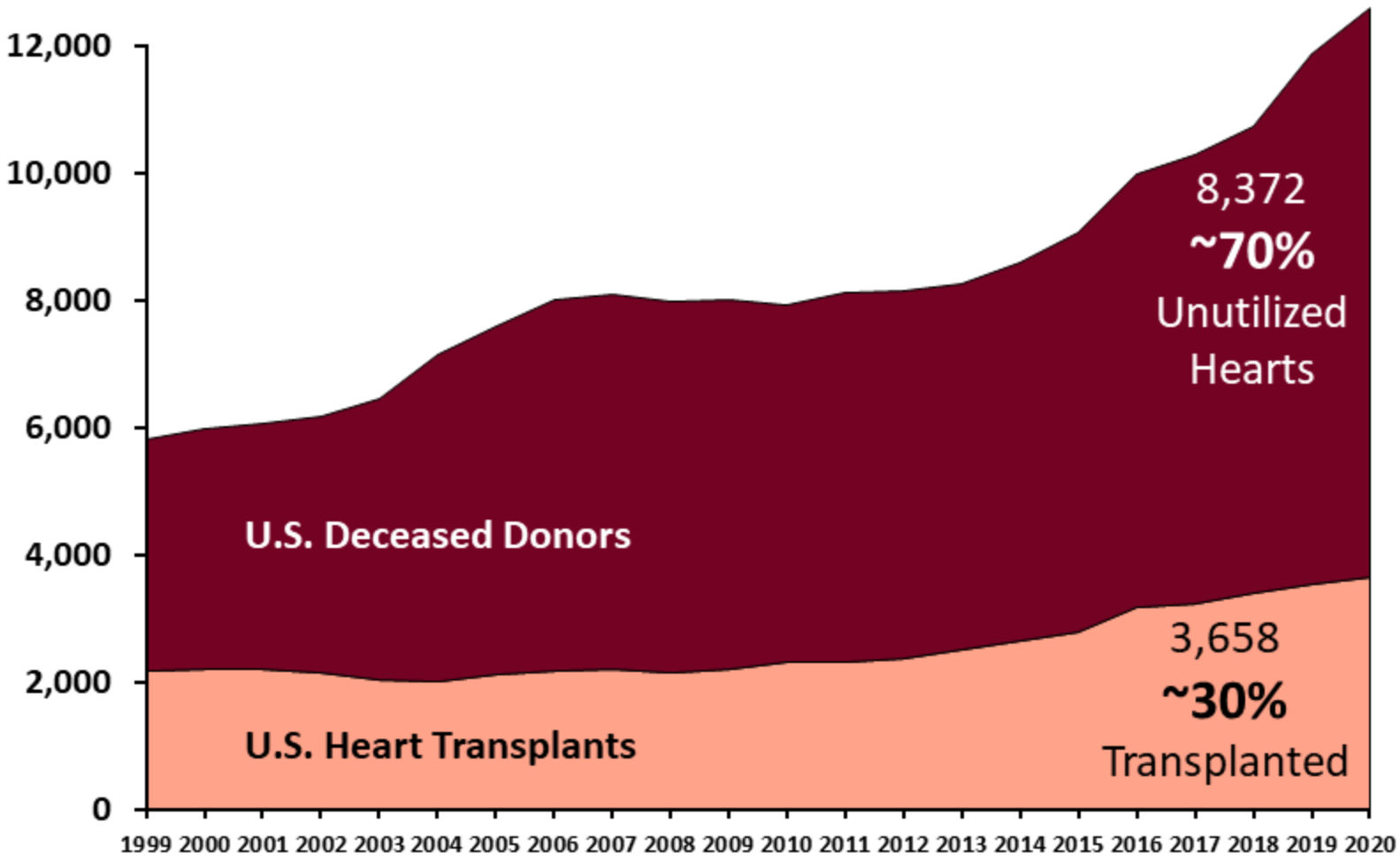
Waleed Hassanein, MD
President and CEO
TransMedics

TransMedics Introduction



- Founded in 1998 to develop Organ Care System (OCS™) technology to increase donor organ utilization for transplantation and improve post-transplant clinical outcomes
- Clinically driven organization that pioneered concept of extracorporeal perfusion of donor hearts, lungs, and livers for transplantation
  - Sponsored 8 US FDA pivotal trials
- The OCS is developed and manufactured in US
  - OCS Lung FDA approved
  - OCS Liver under review by FDA
  - OCS Heart approved internationally and > 1,000 cases transplanted to date worldwide

Only ~30% of Donor Hearts Are Used for Heart Transplants

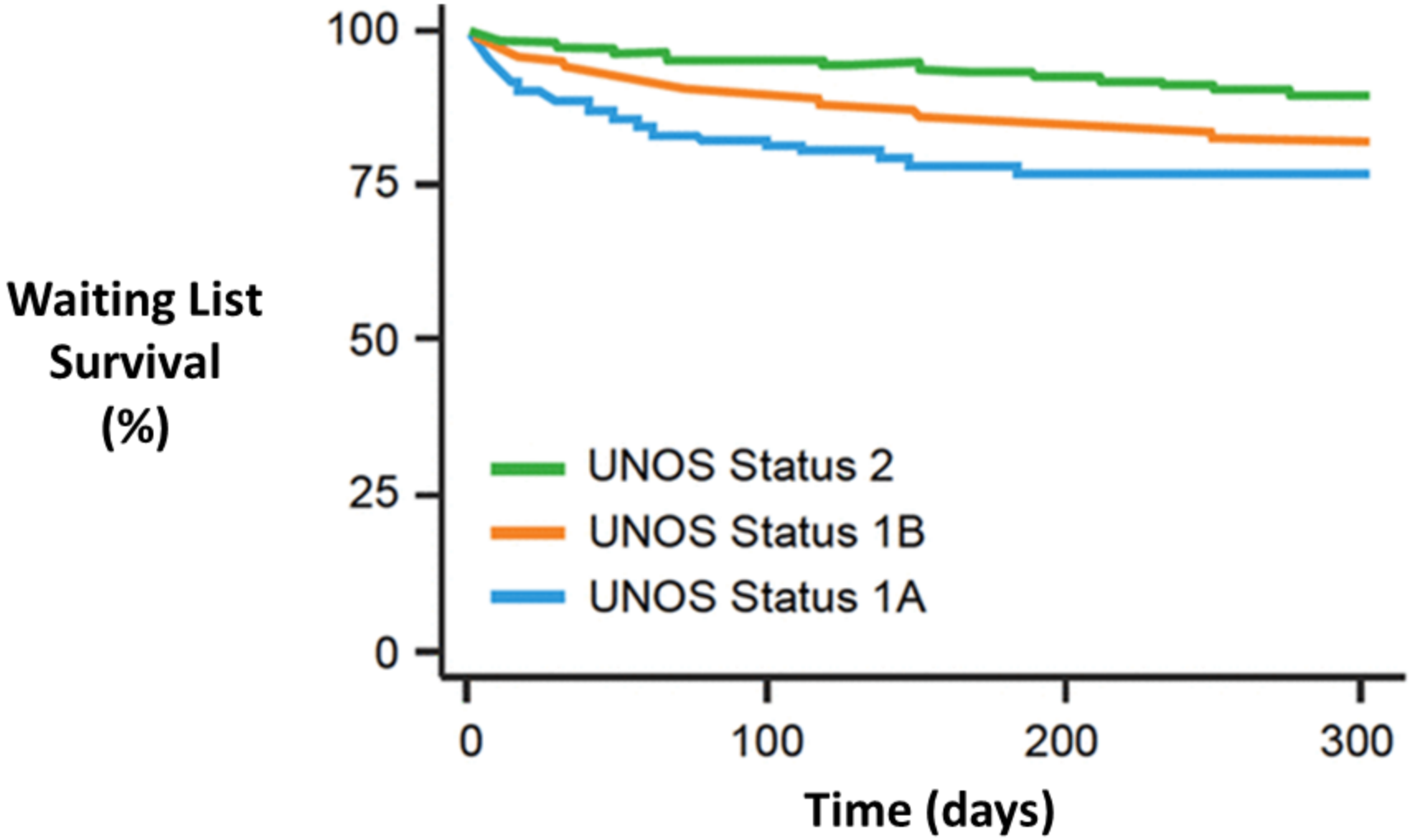


Significant underutilization of deceased donor hearts

Limiting access to patients in need for heart transplantation

Patients waiting are not guaranteed a heart

Longer Wait Times Associated with Higher Mortality



Stehlik et al, Circ Heart Fail 2017

Cold Storage Limits Utilization of Donor Organs and Shown to Negatively Impact Post-Transplant Outcomes

Cold Storage

- Severe time-dependent injury (ischemia)
- No organ optimization capabilities
- No assessment of organ viability

Only 3 out of 10 DBD hearts used[1]

Primary Graft Dysfunction (PGD)

1. 2019 OPTN Database for U.S. Heart Transplants; 2. Singh et al, ISHLT 2018; Nicoroa et al, AJT 2018

OCS Heart System: Integrated Portable Platform Designed to Address Limitations of Cold Storage

OCS™ Heart Console

OCS™ Heart Perfusion Set

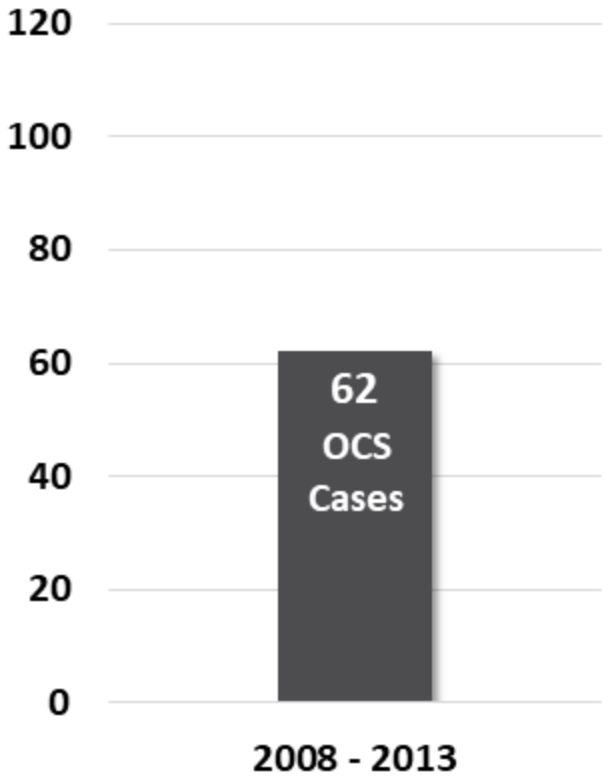
OCS™ Heart Solutions

VIDEO

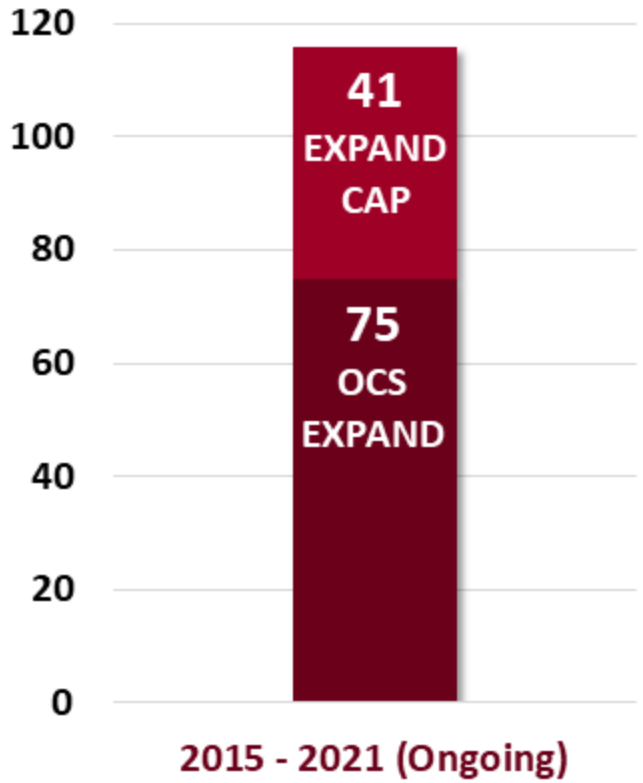
Evolution of OCS Heart – 3 FDA Pivotal Trials for 3 Different Clinical Indications

Primary Dataset for this PMA

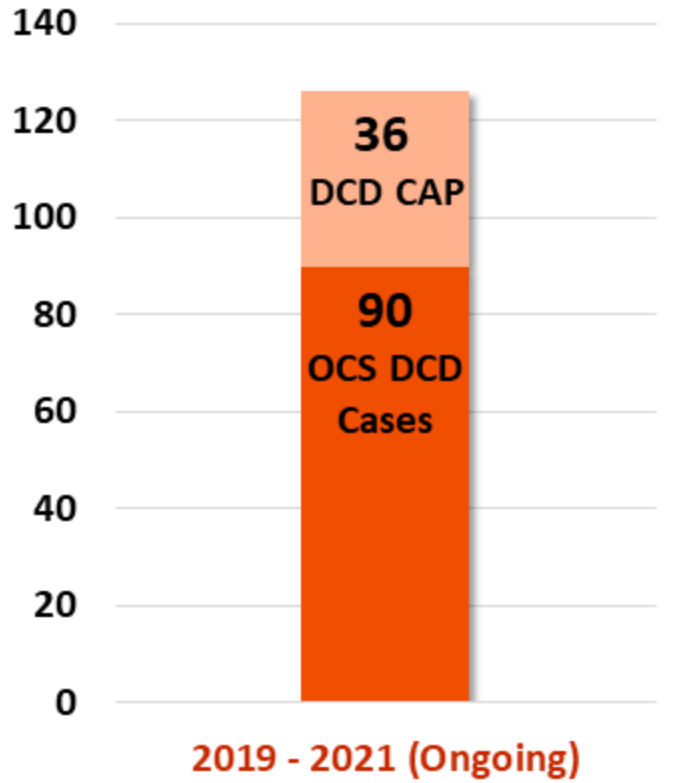
OCS PROCEED II Trial – Standard-Criteria Heart Donors



OCS Heart EXPAND + CAP Trials – Extended-Criteria Heart Donors



OCS Heart DCD + CAP Trials – DCD Heart Donors



Proposed Indication for Use Consistent with Study Criteria

The TransMedics® Organ Care System (OCS™) Heart System is a portable extracorporeal heart perfusion and monitoring system indicated for the resuscitation, preservation, and assessment of donor hearts intended for a potential transplant recipient in a near-physiologic, normothermic and beating state. OCS Heart is indicated for donor hearts with one or more of the following characteristics:

- Expected cross-clamp or ischemic time ≥ 4 hours due to donor or recipient characteristics (e.g., donor-recipient geographical distance, expected recipient surgical time); or
- Expected cross-clamp or ischemic time ≥ 2 hours AND one or more of the following:
  - Donor Age ≥ 55 years; or
  - Donors with history of cardiac arrest and downtime ≥ 20 minutes; or
  - Donor history of alcoholism; or
  - Donor history of diabetes; or
  - Donor Left Ventricle Ejection Fraction (LVEF) ≤ 50% but ≥ 40%; or
  - Donor history of Left Ventricular Hypertrophy (LVH) (septal or posterior wall thickness of > 12 ≤ 16 mm); or
  - Donor angiogram with luminal irregularities but no significant coronary artery disease (CAD)

Overview of Heart EXPAND + CAP Results

- Primary effectiveness endpoint met in EXPAND ($p < 0.0001$)
- **84%** of extended-criteria donor hearts **(refused an average of 60 times)** were successfully transplanted using the OCS Heart System
- **8%** ISHLT severe PGD well below rates reported in literature
- **97%** all-cause patient survival at 30-days post-transplant is comparable to routine heart transplant outcomes (96%; Colvin et al, 2020)
- **92% & 87%** **all-cause** patient survival at 6 & 12 months, respectively

  96% **cardiac-related** patient survival at both 6 & 12 months

Agenda

Clinical Need to Expand Donor Heart Utilization	**Maryjane Farr, MD** Associate Professor of Medicine, Division of Cardiology Medical Director, Adult Heart Transplant Program Columbia University Medical Center / New York-Presbyterian Hospital
Heart EXPAND & EXPAND CAP Trials	**Jacob Schroder, MD** Assistant Professor of Surgery Surgical Director, Heart Transplantation Program Duke University School of Medicine
PROCEED II Trial Summary	**Waleed Hassanein, MD**
Statistical Considerations for Long-Term Survival Modeling	**Chris Mullin, MS** Director, Product Development Strategy, NAMSA
TransMedics Position on FDA Questions Training & Post-Approval Programs	**Waleed Hassanein, MD**
Clinical Perspective & Benefit-Risk Assessment	**Ashish Shah, MD** Professor of Cardiac Surgery Alfred Blalock Endowed Director and Chairman, Department of Cardiac Surgery Vanderbilt University Medical Center

Additional Experts

Pathology	**Anthony J Demetris, MD** Starzl Professor of Liver and Transplant Pathology University of Pittsburgh
Regulatory	**Miriam Provost, PhD** Vice President, Global Regulatory Affairs TransMedics, Inc.
Medical Monitor	**John Wallwork, CBE, FRCS, FMedSci** Emeritus Professor, Cardiothoracic Surgery Royal Papworth Hospital, Cambridge University, UK

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Clinical Need to Expand Donor Heart Utilization

Maryjane Farr, MD

Associate Professor of Medicine, Division of Cardiology
Medical Director, Adult Heart Transplant Program

Columbia University Irving Medical Center /
New York-Presbyterian Hospital

End-Stage Heart Failure – Major Public Health Issue

6.5 million adults in U.S. have heart failure[1]

46% increase in heart failure prevalence estimated by 2030[1]

5-10% of patients with heart failure are “end-stage” or “advanced”[1]

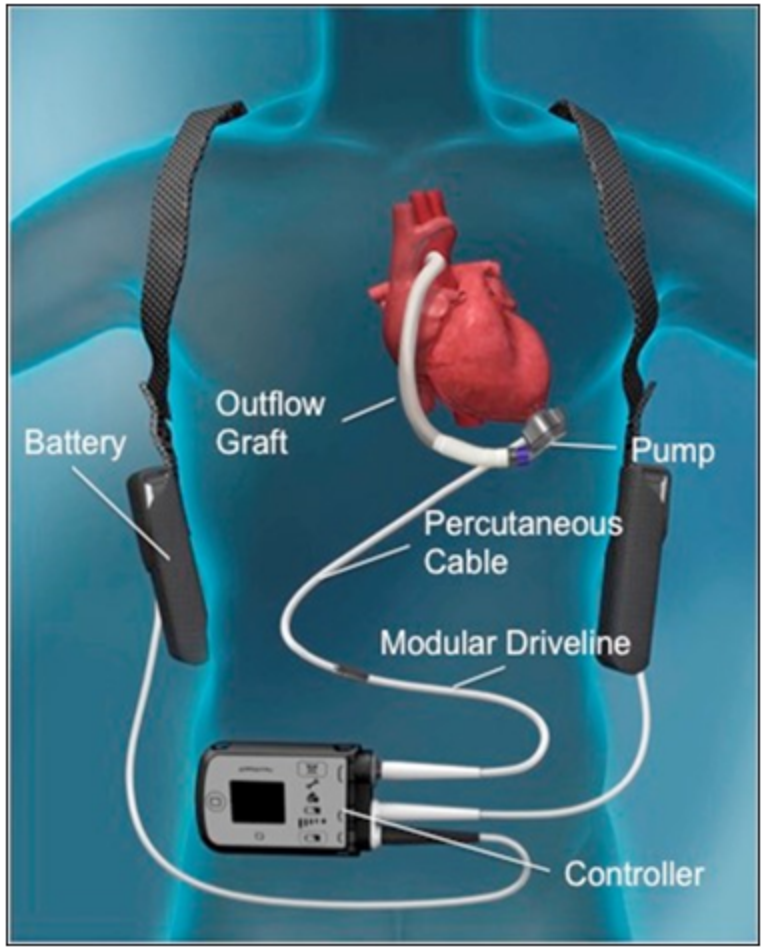
40-60% 1-year mortality rate for patients with end-stage heart failure[2]

1. AHA Statistics 2019; 2. Singh et al, Circ Heart Fail 2012

Durable Left Ventricular Assist Devices Used as Bridge to Heart Transplant

Ventricular Assist Devices (VADs)

- Beneficial for selected patients
  - Bridge to transplant
  - Destination therapy if LV failure only
- 2-year survival HM3 79%
- Complications
  - Stroke 10%
  - Bleeding 24.5%
  - Infection 58.3%
  - Right ventricular failure 34.2%

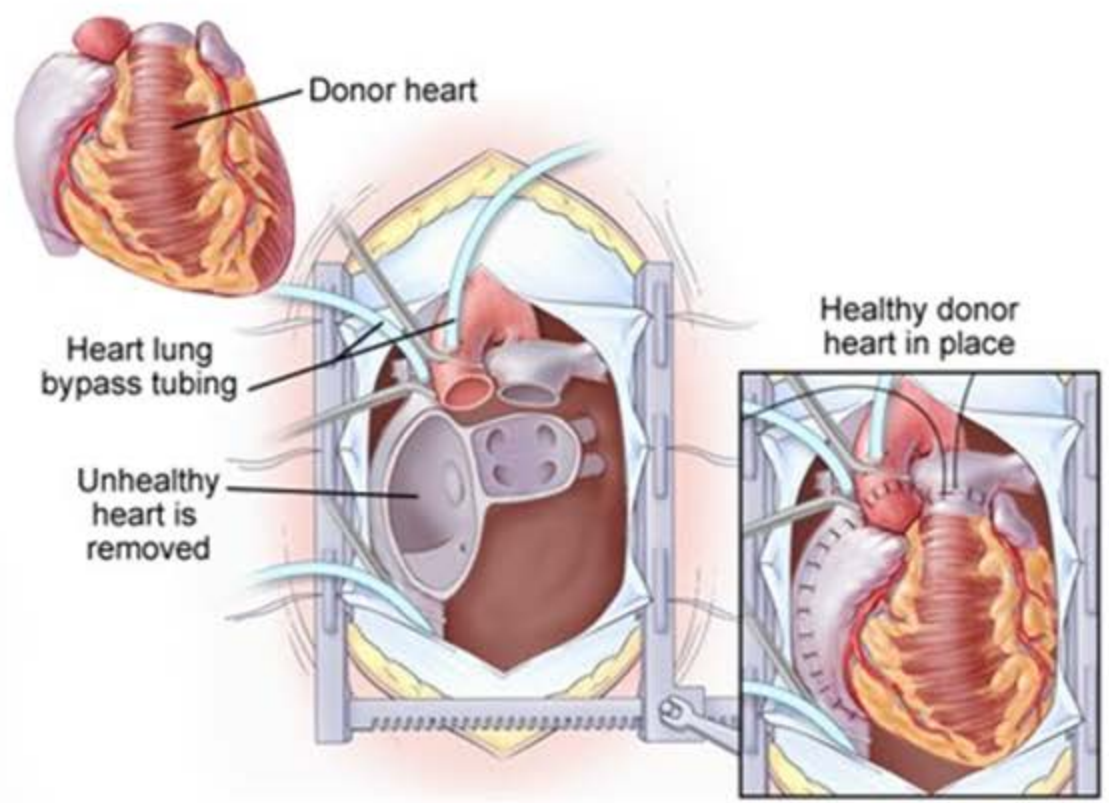


Mehra et al, NEJM 2019

Cardiac Transplant is Gold Standard

Cardiac Transplant

- Definitive replacement therapy
  - Requires intensive long-term care
- 88-92% survival at 1 yr, 72-80% at 5 yrs
- Improves
  - Functional status
  - Health-related quality of life



Yancy et al, Circulation 2013; Colvin et al, Am J Transplant 2020

Heart Transplant Challenges Due to Supply

12,588 deceased organ donors in 2020 in U.S.[1]

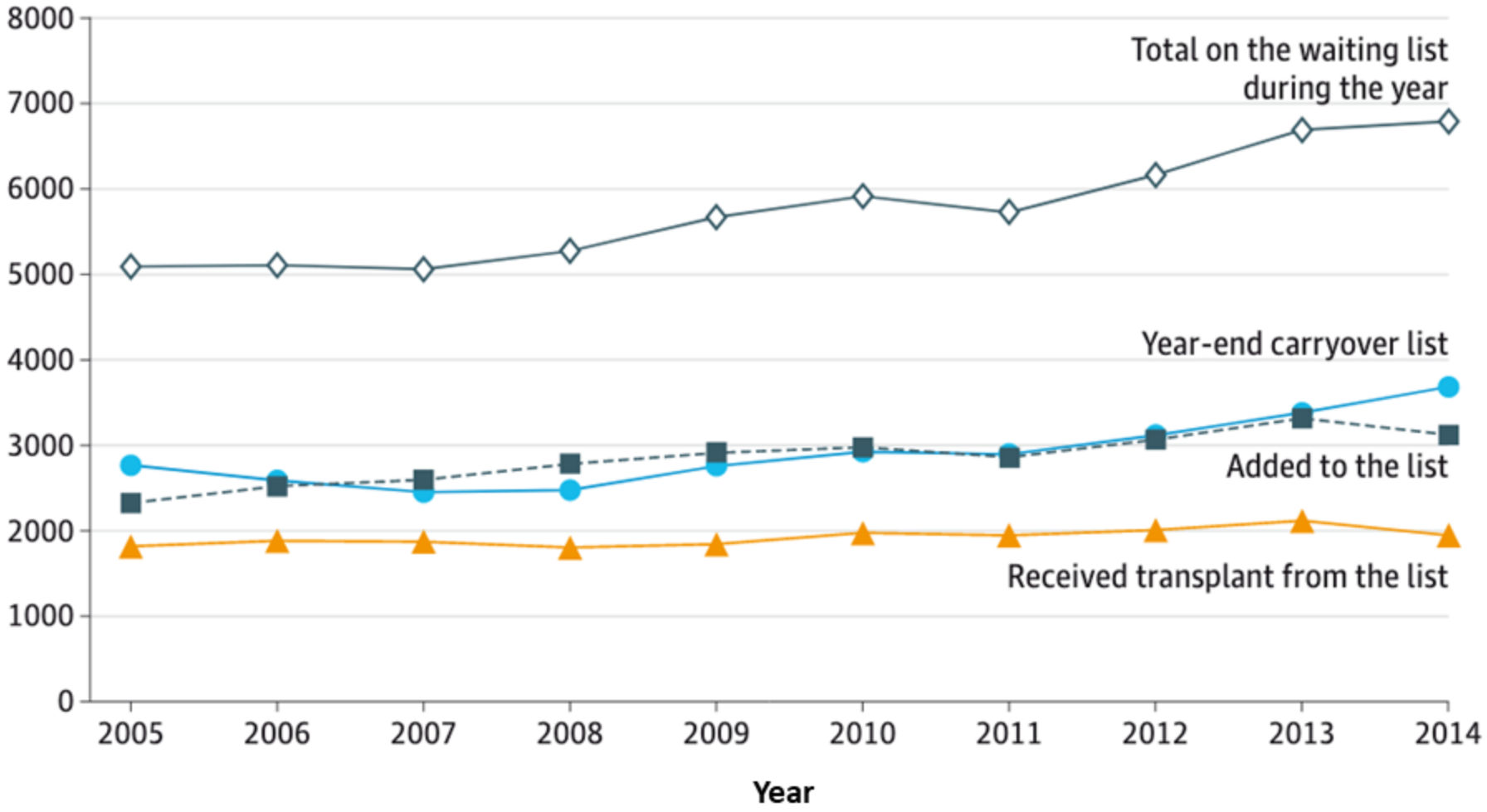
3,658 heart transplants in 2020 in U.S.[1]

Only ~3 hearts out of every 10 donated hearts are used for transplant

1. Scientific Registry of Transplant Recipients and Organ Procurement Network Database

Oversold Transplant Waiting List

Patients Added, Removed, and Waiting for Transplant



Stevenson, JAMA Intern Med 2015

Still Dependent on Cooler Despite Medical Advances

COLD STORAGE

Limitations of Cold Storage

- Donor hearts can only safely be preserved for ~4 hours
- Time-dependent ischemia
- No ability to provide therapeutic intervention to organ
- No ability to assess heart function
- Limited to standard-criteria hearts

Recent Federal Changes Mandate that Organs Be Allocated to Sickest Patients First

- Jan 2020 – UNOS with HHS determined local allocation not consistent with fair access
- Now able to transplant to sickest patients first
  - Longer travel times
  - Longer ischemic times
- Need new technologies to mitigate adverse effects of long ischemic times

Growing Pool of Lost Hearts to DCD Donation

- 2019 – 1,543 DCD donors between ages 18-49 years old
  - ≥ 1 organ (liver, kidney, lung) transplanted
  - Only 7 hearts able to be utilized
    - All successfully transplanted using OCS Heart System in clinical trial (IDE G180272; pivotal trial ongoing)

Unmet Need to Address Limitations of Cold Storage

- Heart transplant is the gold standard therapy for end-stage heart failure
- Cold storage is the only available option for preservation despite severe limitations that restrict utilization to ~3 out 10 donor hearts
- Significant unmet need for new heart preservation technologies to address limitations of cold storage and increase number of life-saving heart transplants

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Heart EXPAND & EXPAND CAP Trials

Jacob Schroder, MD

Assistant Professor of Surgery

Surgical Director, Heart Transplantation Program

Duke University School of Medicine

Heart EXPAND Trial Overview

Objective	Evaluate ability of OCS Heart System to significantly increase utilization of donor hearts that are rarely transplanted today due to limitations of cold storage
Target Enrollment	Extended-criteria donor hearts in typical heart recipients
Trial Design	Single-arm, multicenter U.S. clinical trial

Why a Single-Arm Trial

- Unethical to randomize extended-criteria donor hearts to cold storage
- Concurrent controls would be of limited clinical value as this is a different donor heart population

Donor Heart Eligibility Criteria

- Expected total cross-clamp time ≥ 4 hours; OR
- Expected total cross-clamp time ≥ 2 hours plus ≥ 1 additional risk factor
  - Donor age 45-55 years with no coronary catherization data
  - Donor age ≥ 55 years
  - Left ventricular septal or posterior wall thickness of > 12 and ≤ 16 mm
  - Reported down time of ≥ 20 min with stable hemodynamics at final assessment
  - Left heart ejection fraction 40-50%
  - Donor angiogram with luminal irregularities with no significant CAD
  - History of carbon monoxide poisoning with good cardiac function at time of donor assessment
  - Social history of alcoholism with good cardiac function at time of donor assessment
  - History of diabetes with negative coronary angiogram for CAD

Donor Heart on OCS Transplant Acceptance Criteria

- OCS arterial lactate levels < 5 mmol/L at end of OCS perfusion period with stable lactate trend
- Recommended ranges for OCS heart perfusion parameters after stabilization
  - Coronary flow (CF) 400-900 mL/min
  - Aortic pressure (AOP) 40-100 mmHg
- Clinically satisfied with donor heart evaluation on OCS

Recipient's Surgical Procedure Should Not Be Initiated Until Donor Heart Accepted on OCS

Role of OCS Parameters and Clinical Judgment in Donor Heart Acceptance

- Arterial lactate is an important biomarker for myocardial ischemia
- Prospective analysis of OCS perfusion parameters to predict graft failure[1]
  - First 49 patients transplanted on OCS with standard-criteria hearts
  - Lactate trend, rate of change, and ending lactate had high sensitivity and specificity
  - 5 mmol/L limit for standard-criteria hearts (baseline lactate ≤ 1 mmol/L)
- In EXPAND, a stable lactate trend added as qualifier because extended-criteria hearts may have higher starting lactate values (eg, 3-4 mmol/L)
  - Some hearts turned down in EXPAND because lactate increased despite attempts to maximize perfusion and AOP (certain cases where absolute lactate < 5 mmol/L)
- Other OCS parameters and clinical judgement also used to determine transplantability
- Providing additional data to inform clinical judgment is benefit of OCS not a risk

1. Hamed et al, JHLT 2009

Recipient Inclusion and Exclusion Criteria

Recipient Inclusion Criteria

- Registered male or female primary heart transplant candidate
- Age ≥ 18 years
- Provided informed consent

Recipient Exclusion Criteria

- Prior solid organ or bone marrow transplant
- Chronic use of hemodialysis or diagnosis of chronic renal insufficiency
- Multi-organ transplant required

Primary Effectiveness and Safety Endpoints

- Primary effectiveness composite endpoint
  - Survival at Day 30
  - Absence of ISHLT severe PGD in first 24 hours
  - Performance goal of 65% (assumed rate of 80%)
- Primary safety endpoint
  - Incidence of heart graft-related SAEs (HGRSAEs) in first 30 days

Rationale for Performance Goals in EXPAND

- No published literature on rate of PGD in extended-criteria donor heart transplants
- Higher range of published PGD of ~30% added to the 5% rate of 30-day mortality for standard-criteria hearts to derive the 65% PG
- With sample size of 75 patients, success rate assumed to be 80% to meet 65% PG
- No prior data on moderate and severe ISHLT PGD through 30 days post transplant
- Primary effectiveness endpoint includes safety components (survival and PGD)

Secondary Endpoints

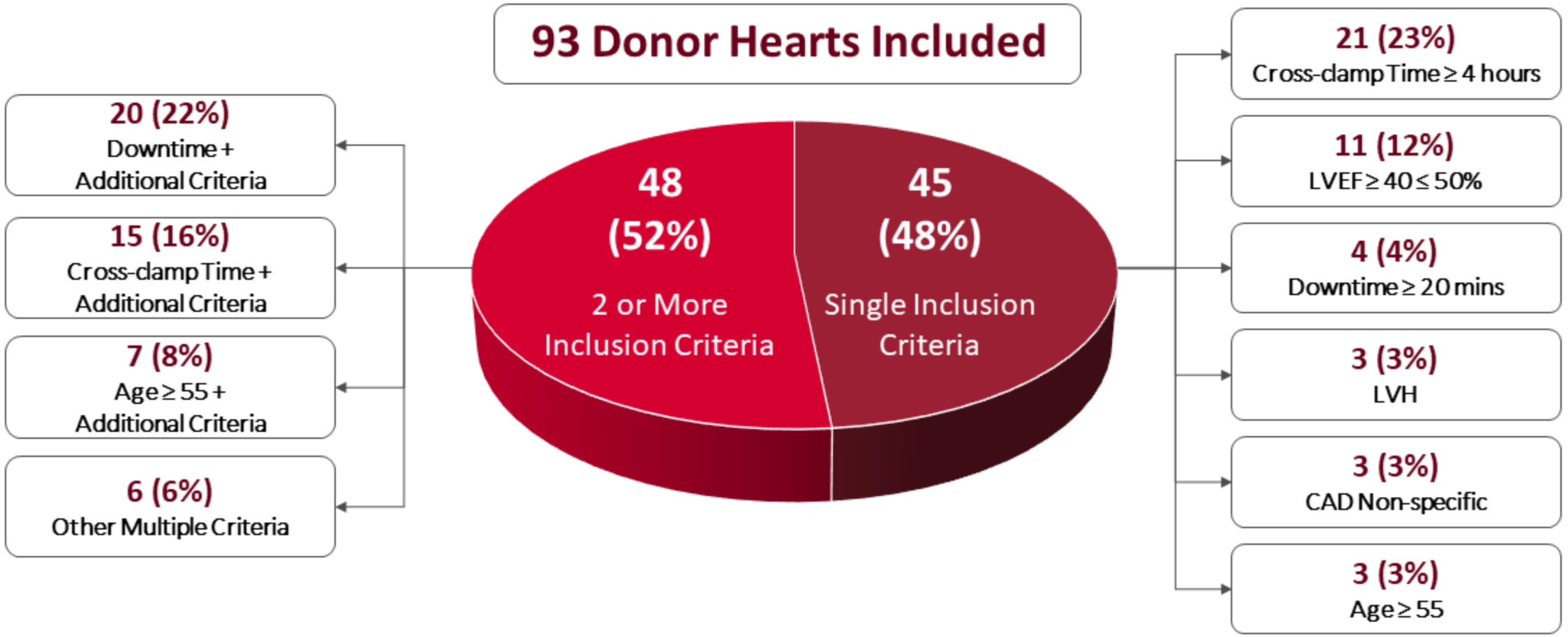
- Patient survival at Day 30
- Incidence of severe PGD in first 24 hours
- Rate of donor heart utilization for transplantation

PGD Assessment and Adjudication

- Moderate or severe PGD defined in protocol according to ISHLT consensus recommendations

- Clinical events independently adjudicated by medical monitor
  - Dr. John Wallwork
    Founding Member and Past President, ISHLT
    Emeritus Professor of Cardiothoracic Surgery, Papworth Hospital and Cambridge University

Donor Heart Risk Factors for EXPAND Trial Inclusion – 52% of Donors Had 2 or More Risk Factors

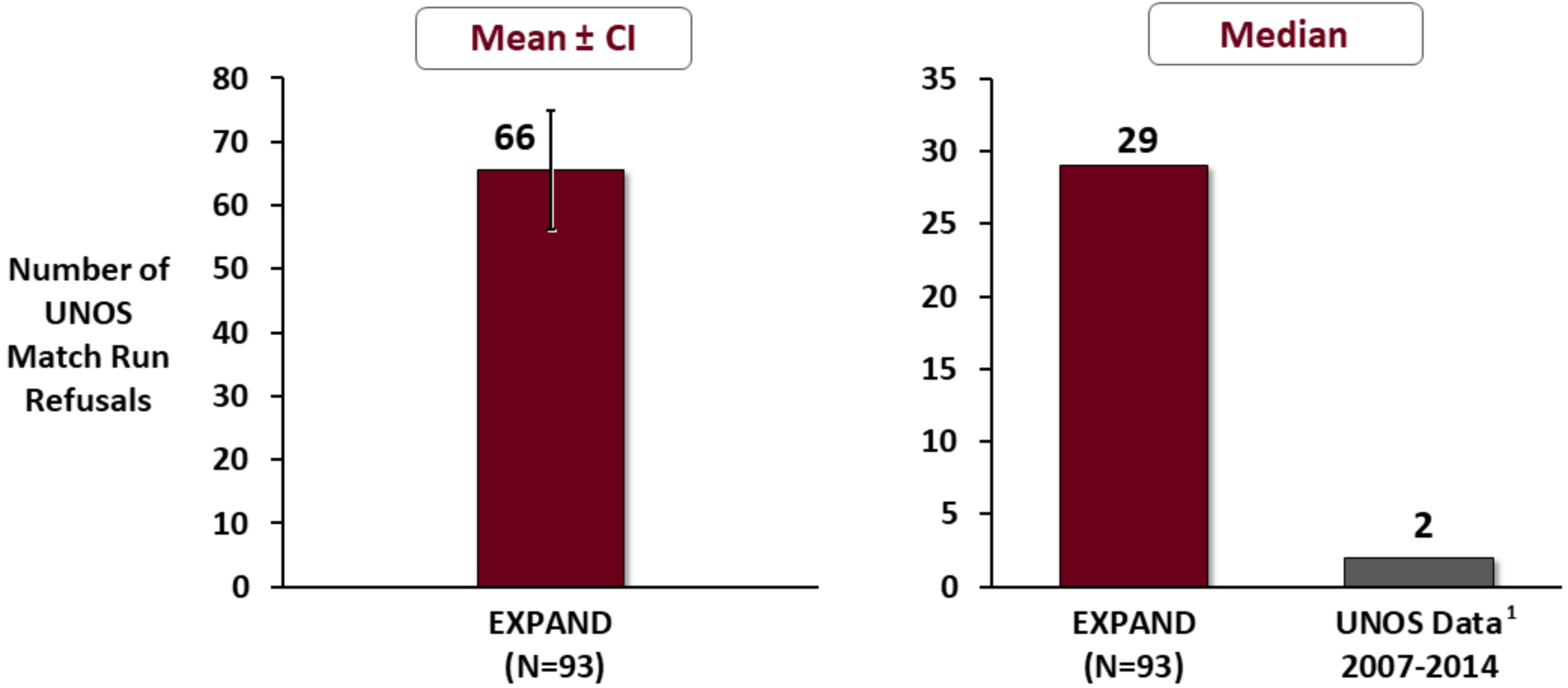


UNOS Heart Transplant Database Validated EXPAND Criteria Are Seldomly Utilized in the U.S.

Donor Risk Factors / Inclusion Criteria	OCS EXPAND (N=93)	UNOS SRTR Data* (N=10,426)	p-value
Expected cross-clamp time ≥ 4 hours	37 (39.8%)	1,607 (15.4%)	< 0.0001
Downtime ≥ 20 minutes	33 (35.5%)	240 (2.3%)	< 0.0001
LVEF ≥ 40% and ≤ 50%	24 (25.8%)	481 (4.6%)	< 0.0001
Donor age ≥ 55 years	11 (11.8%)	295 (2.8%)	< 0.0001
LVH >12 ≤ 16 mm	18 (19.4%)	Not collected	
2 or More Risk Factors / Inclusion Criteria			
Cross-clamp ≥ 4 hours plus other factors	13 (14.0%)	464 (4.5%)	0.0003
Downtime ≥ 20 minutes plus other factors	9 (9.7%)	58 (0.6%)	< 0.0001
Donor age ≥ 55 years plus other factors	7 (7.5%)	104 (1.0%)	< 0.0001

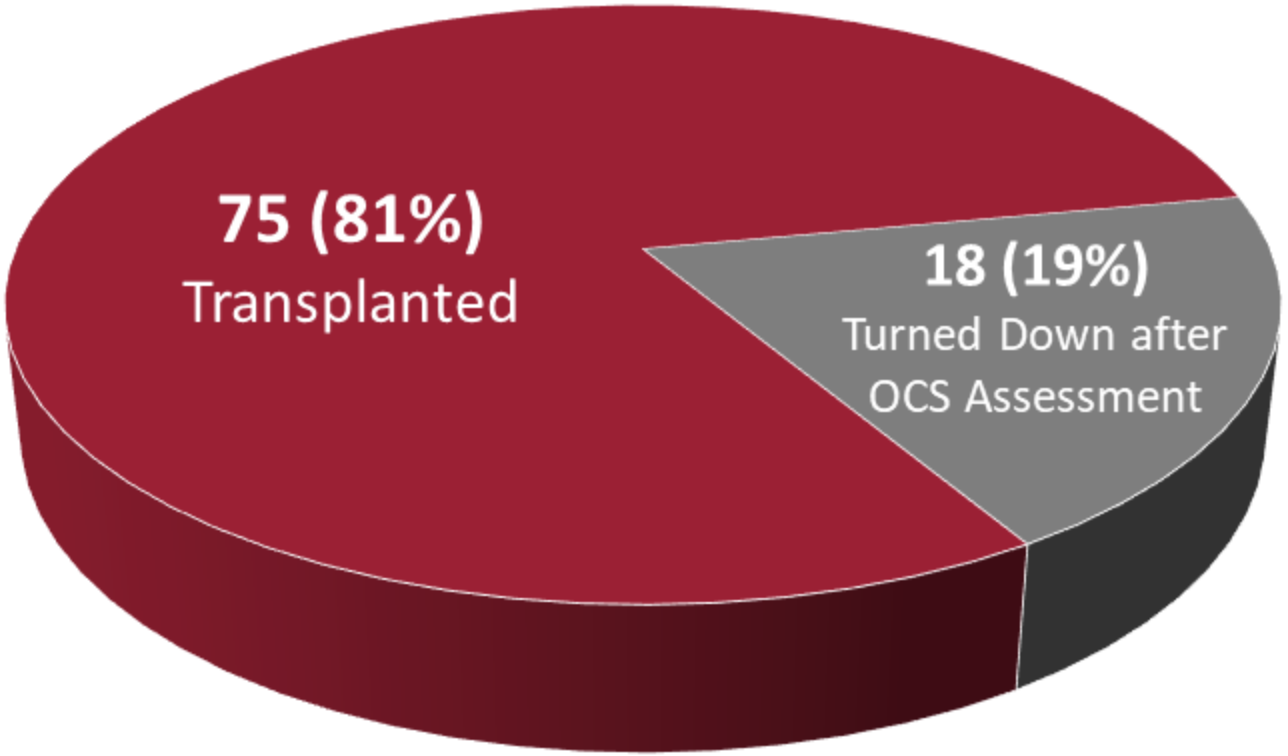
*Data from 2015-2018 US Heart Transplant Registry

EXPAND Enrolled Donor Hearts with Significantly More Match Run Refusals



1. Baran et al, Circ Heart Fail 2019

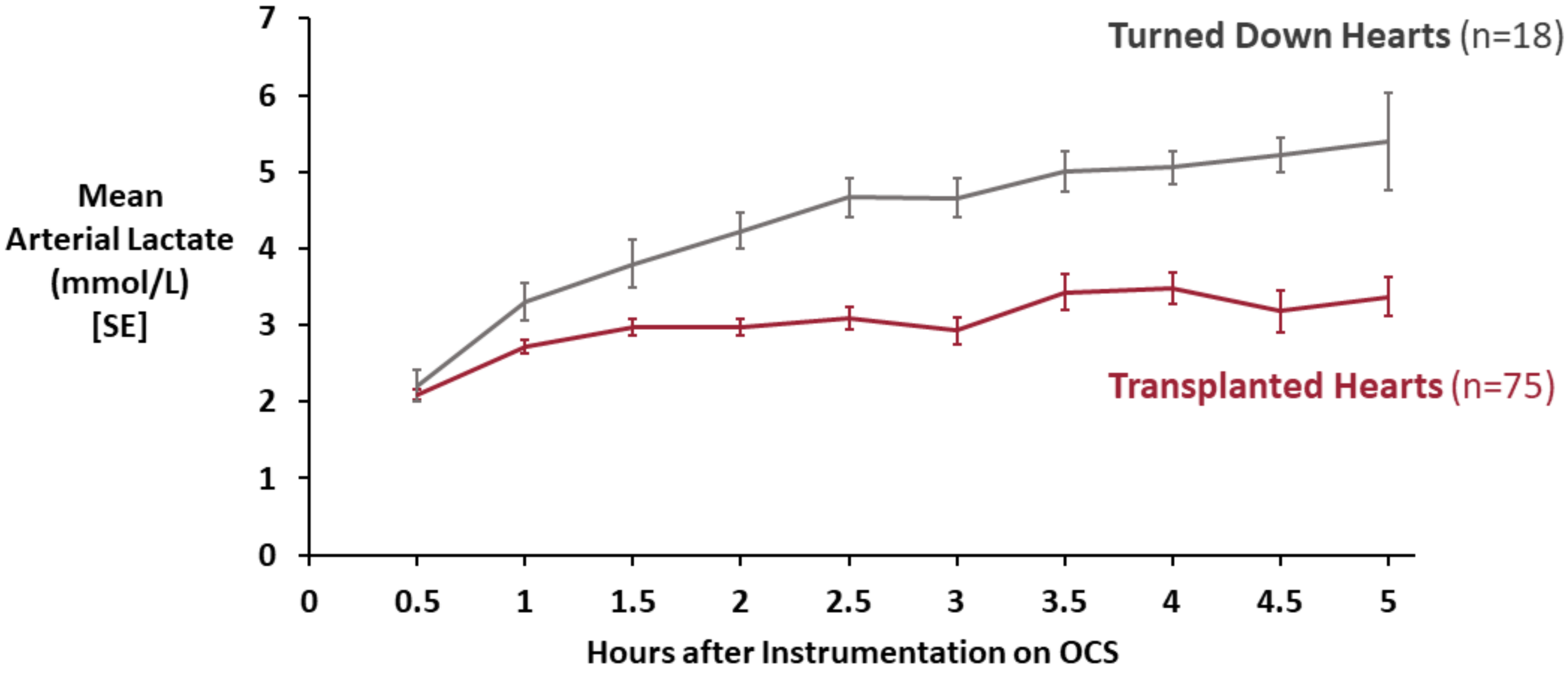
81% of Donor Hearts Utilized for Transplantation



Reasons for Turn Down on OCS

- Continuous rising lactate and final lactate ≥ 5 mmol/L (n=8)
- Continuous rising lactate (n=7)
- Continuous rising lactate and RV dysfunction (n=2)
- Continuous rising lactate and inability to wean off pacing (n=1)

Arterial Lactate Trend Served as a Key Indicator for Assessment of Donor Hearts on OCS



Demographics and Baseline Characteristics of Transplanted Recipient Population

Recipient Characteristics	(N=75)
Baseline Characteristics	
Age (years), mean ± SD	55.5 ± 12.6
Male, n (%)	61 (81%)
BMI (kg/m^2), mean ± SD	27.7 ± 4.7
Risk Factors, n (%)	
Age > 65	18 (24%)
History of mechanical circulatory support	48 (64%)
Female donor to male recipient mismatch	12 (16%)
Renal dysfunction	11 (15%)
Status, n (%)	
Status 1A	52 (69%)
Status 1B	22 (29%)
Status 2	1 (1%)

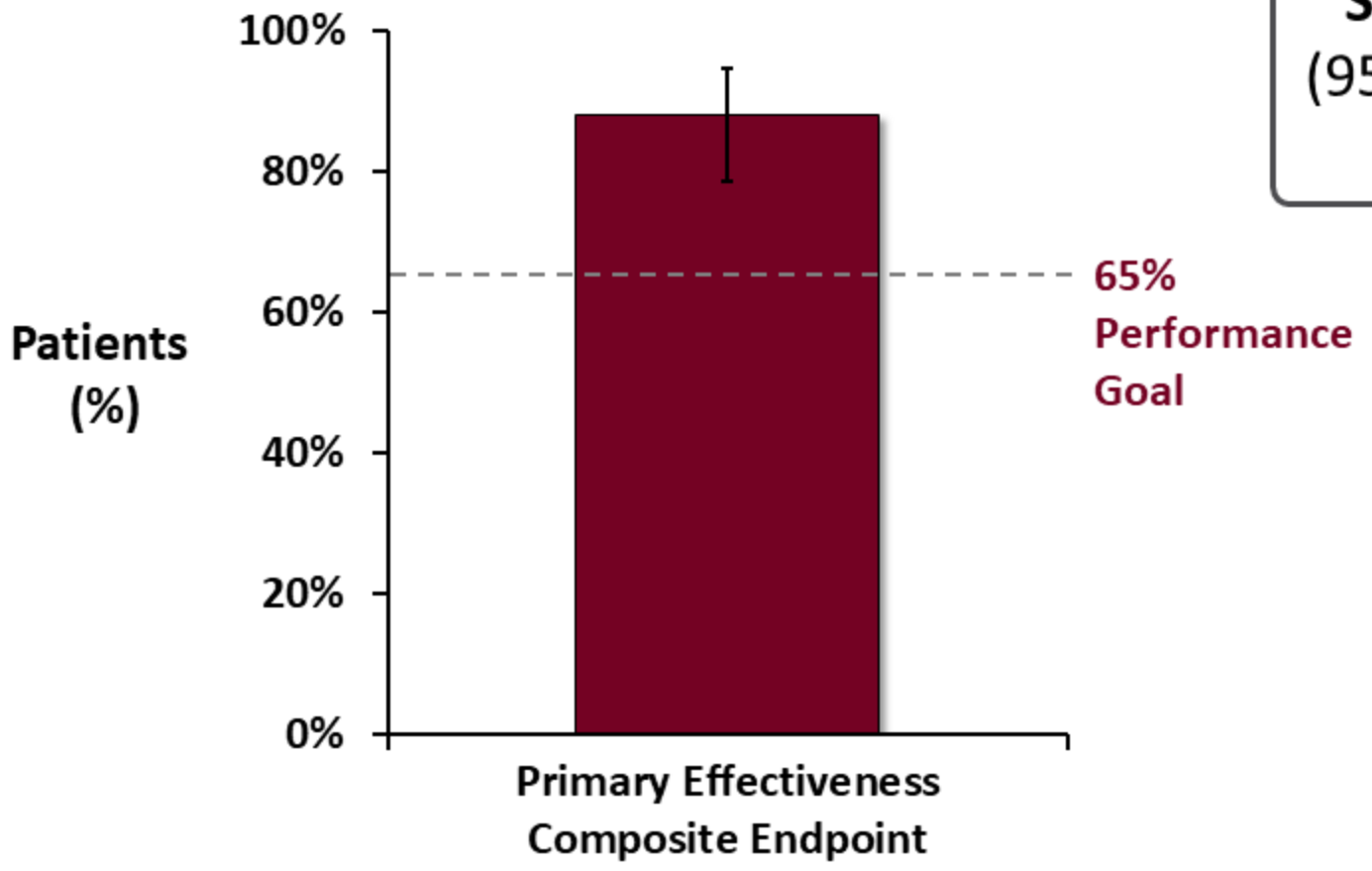
Donor Heart Preservation Characteristics

Parameter	Transplanted Donor Hearts (N=75)
Cross-clamp time (hours)	
Mean ± SD	**6.3 ± 1.6**
Min – Max	**2.9 – 11.4**
Cold ischemic time (hours)	
Mean ± SD	**1.7 ± 0.4**
Min – Max	**1.1 – 2.8**

85% of hearts transplanted in US < 4 hour maximum with cold storage*

*SRTR database

Primary Effectiveness Endpoint Met



Success Rate: 88.0%
(95% CI: 78.4% - 94.4%)
p < 0.0001

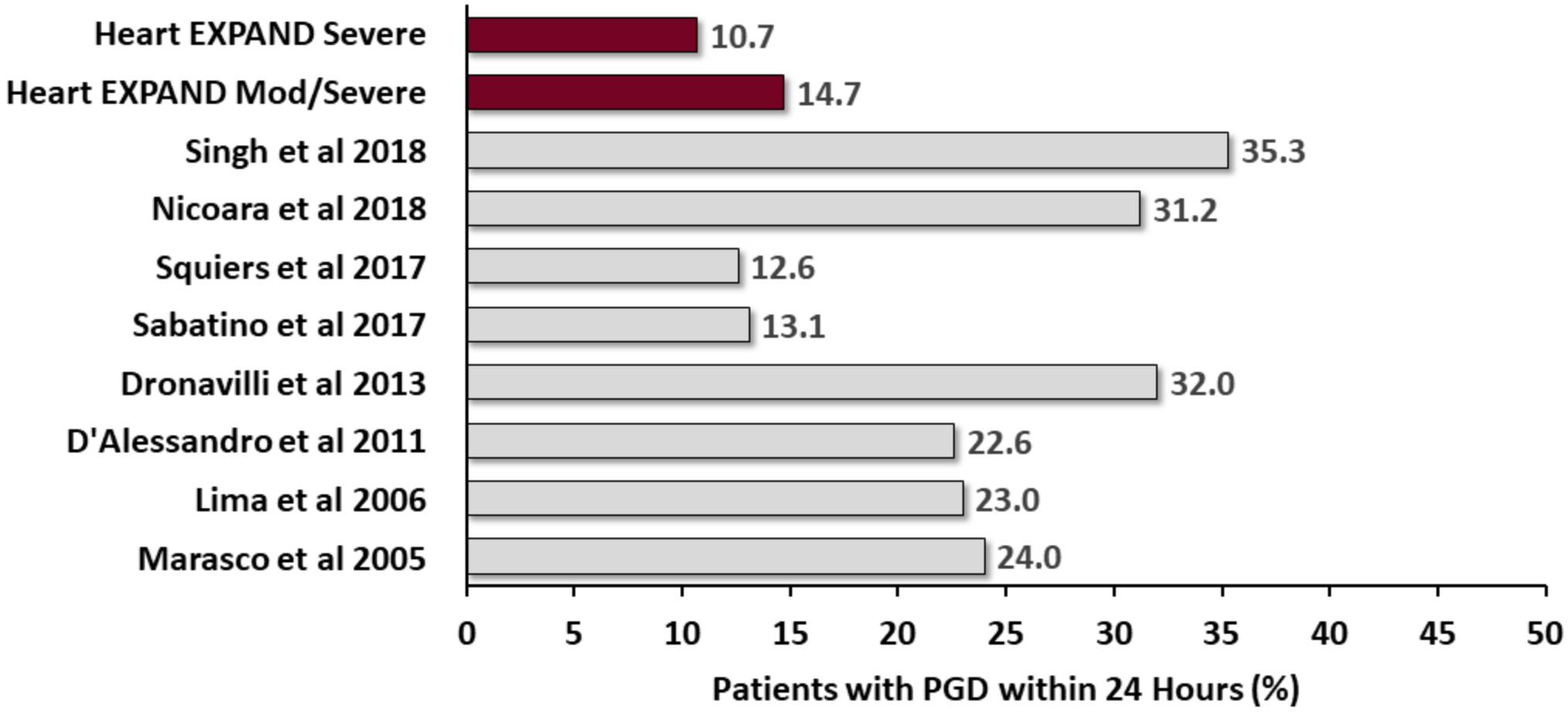
(30-day survival and freedom from severe ISHLT PGD)

Favorable Results on Secondary Endpoints

Secondary Endpoints (Components of Primary Composite Endpoint)	(N=75)
Patient survival at day 30 post transplantation	
Proportion (n/N)	**94.6% (70/74*)**
Severe PGD (left or right ventricle) in first 24 hours post transplantation	
Proportion (n/N)	**10.7% (8/75)**

*One patient had graft failure requiring re-transplant

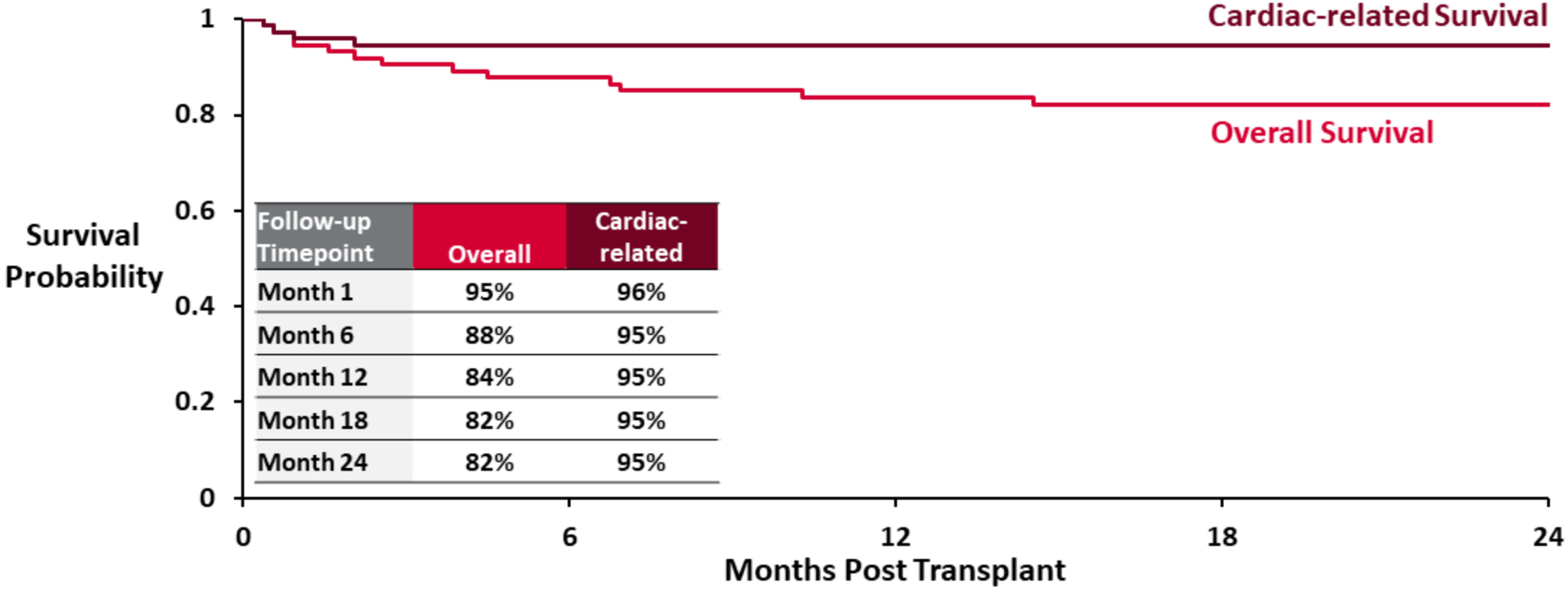
PGD with OCS Heart Similar or Lower than Other Studies



Important Considerations for Assessing Mortality in Heart Transplantation

- Most patients undergoing heart transplant are not otherwise healthy
  - Majority previously on VADs with associated complications
  - On long-term immunosuppressives
- Mortality in initial post-transplant period likely related to transplant procedure or cardiac graft
- After initial post-transplant period, recipients subject to competing risks for non-cardiac causes of death
- Cardiac-related survival is a clinically appropriate endpoint to assess preservation technology

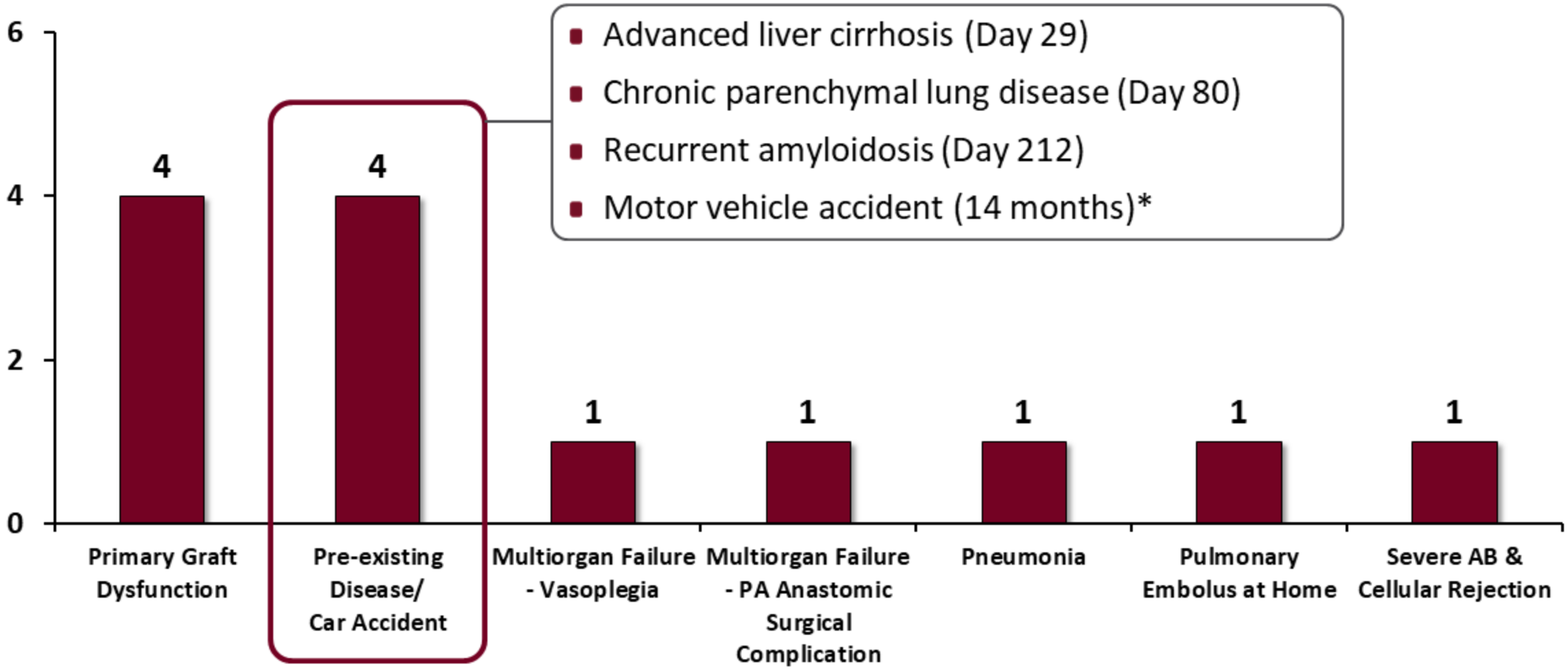
All-Cause and Cardiac-Related Long-Term Survival



Follow-up Timepoint	Overall	Cardiac-related
Month 1	95%	96%
Month 6	88%	95%
Month 12	84%	95%
Month 18	82%	95%
Month 24	82%	95%

Month	0	1	6	12	18	24
Overall	75	70	65	59	50	30
Cardiac-related	75	70	65	59	50	30

Causes of Death in EXPAND Trial



* This death was outside of the adjudication window; however, the original death note was obtained from the site

Low Incidence of Primary Safety Endpoint Events

	(N=75)
Primary safety endpoint	
Mean ± SD	**0.2 ± 0.37**
HGRSAEs by type	
Moderate or severe PGD, n/N (%)	**11/75 (14.7%)**
Primary graft failure requiring re-transplantation	**1/75 (1.3%)**

HGRSAE = heart graft-related serious adverse event

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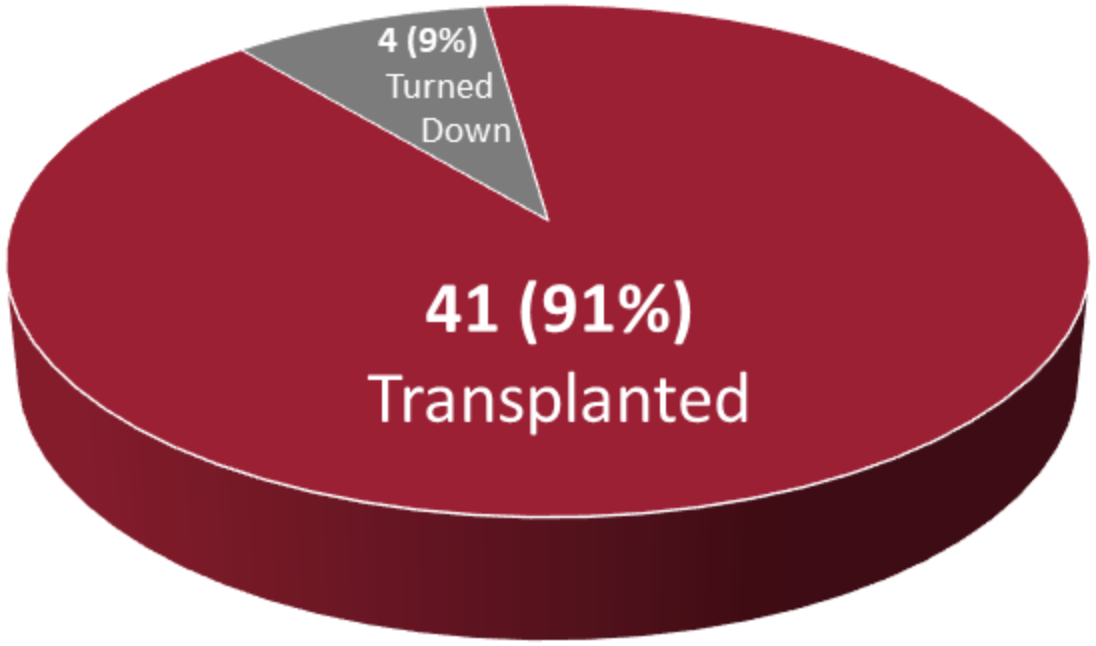
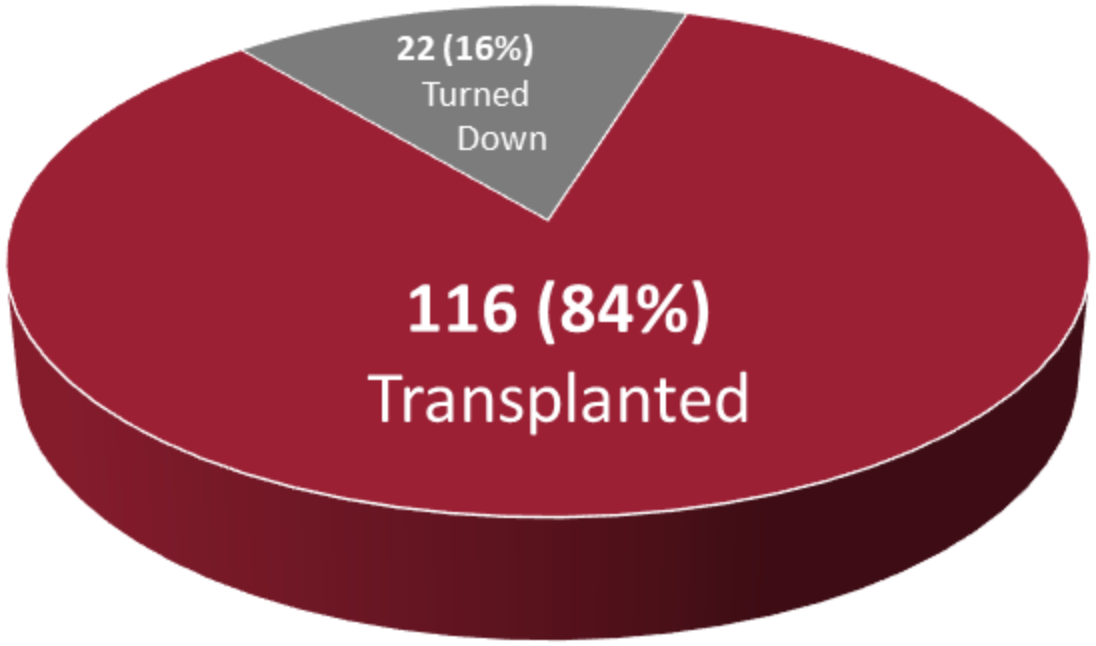
EXPAND CAP & Pooled EXPAND + CAP Analyses

Findings from EXPAND Continued Access Protocol Further Support Effectiveness and Safety of OCS Heart System



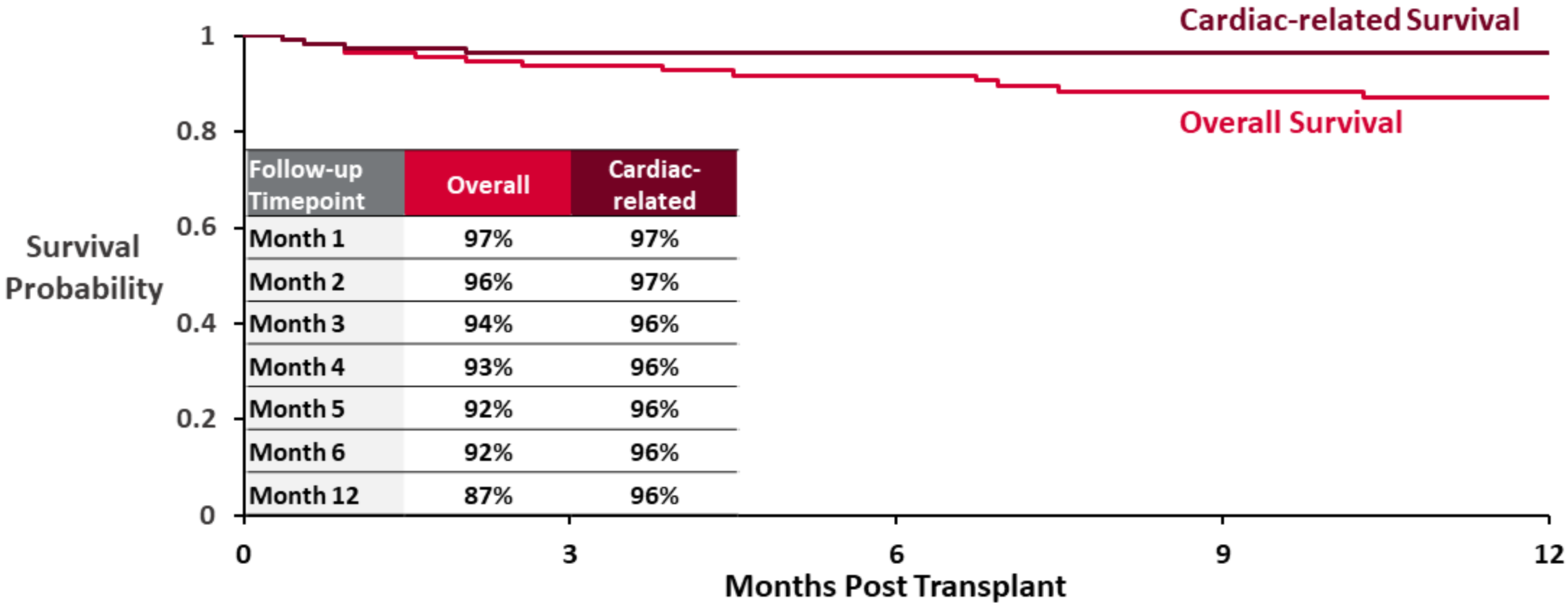
- **41** Patients with ≥ 30-day follow-up
- **91%** Utilization for transplantation
- **100%** 30-day survival
- **2.4%** Incidence of severe PGD

Pooled Results from EXPAND + CAP Support Effectiveness and Safety of OCS Heart System



- **116** Patients
- **84%** Utilization for transplantation
- **97%** 30-day survival
- **8%** Incidence of severe PGD

Pooled EXPAND + CAP Long-Term Survival



Follow-up Timepoint	Overall	Cardiac-related
Month 1	97%	97%
Month 2	96%	97%
Month 3	94%	96%
Month 4	93%	96%
Month 5	92%	96%
Month 6	92%	96%
Month 12	87%	96%

Month	0	1	2	3	4	5	6	12
Overall	116	111	100	98	97	96	85	65
Cardiac-related	116	111	100	98	97	96	85	65

Data from EXPAND + CAP Trials Provide Substantial Evidence of Safety and Effectiveness of OCS Heart System

- Primary effectiveness endpoint met in EXPAND ($p < 0.0001$)
- **84%** of extended-criteria donor hearts **(refused an average of 60 times)** were successfully transplanted using the OCS Heart System
- **8%** ISHLT severe PGD well below rates lower reported in literature
- **97%** all-cause patient survival at 30-days post-transplant is comparable to routine heart transplant outcomes (96%; Colvin et al, 2020)
- **92% & 87%** **all-cause** patient survival at 6 & 12 months, respectively

  96% **cardiac-related** patient survival at both 6 & 12 months

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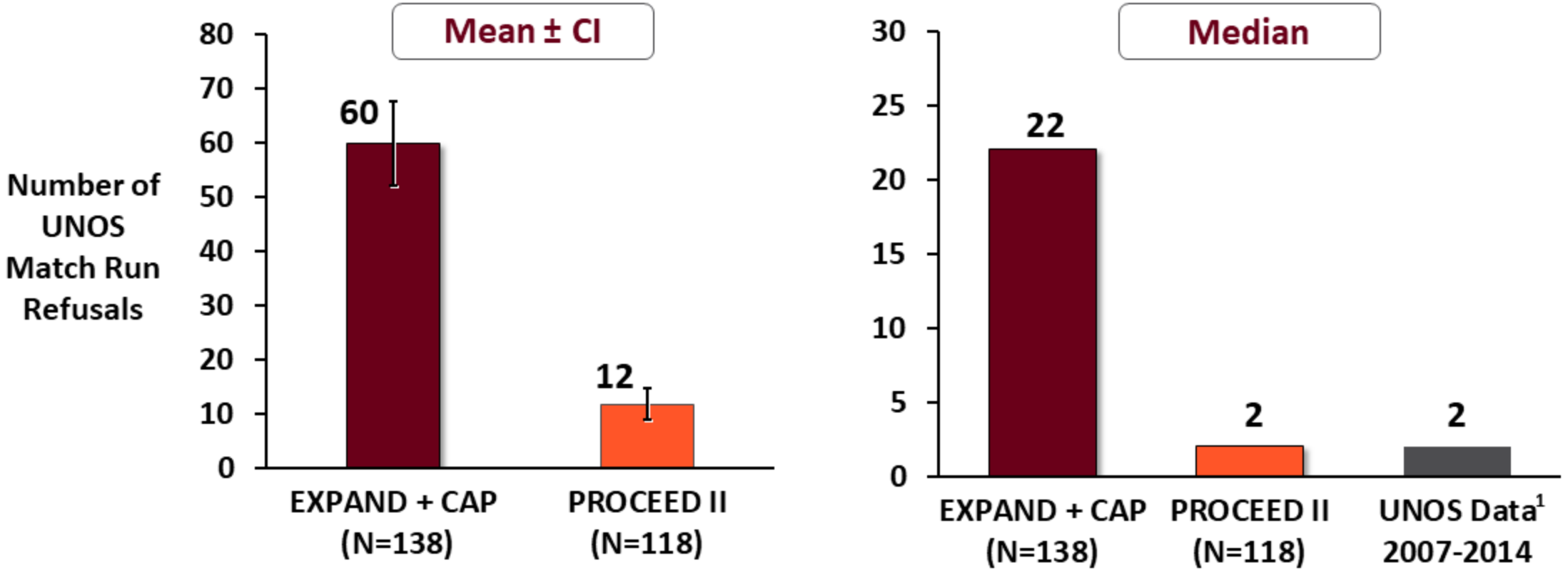
PROCEED II Trial Summary

Waleed Hassanein, MD
President and CEO
TransMedics

PROCEED II – First Trial Designed for Any Ex-Vivo Organ Perfusion Technology and for OCS Heart System

- Designed based on 2001 Celsior cold preservation solution trial design: non-inferiority RCT with 30-day follow-up for standard-criteria hearts
- Met primary effectiveness and safety endpoints
- Unplanned, post-hoc UNOS follow-up revealed increased overall mortality; however comparable cardiac-related mortality in OCS arm vs control
- Substantial differences in device design, use model, and donor and recipient populations limit the utility of PROCEED II data for this PMA

PROCEED II Enrolled Standard-Criteria Donors That Are Substantially Different from EXPAND & CAP Population

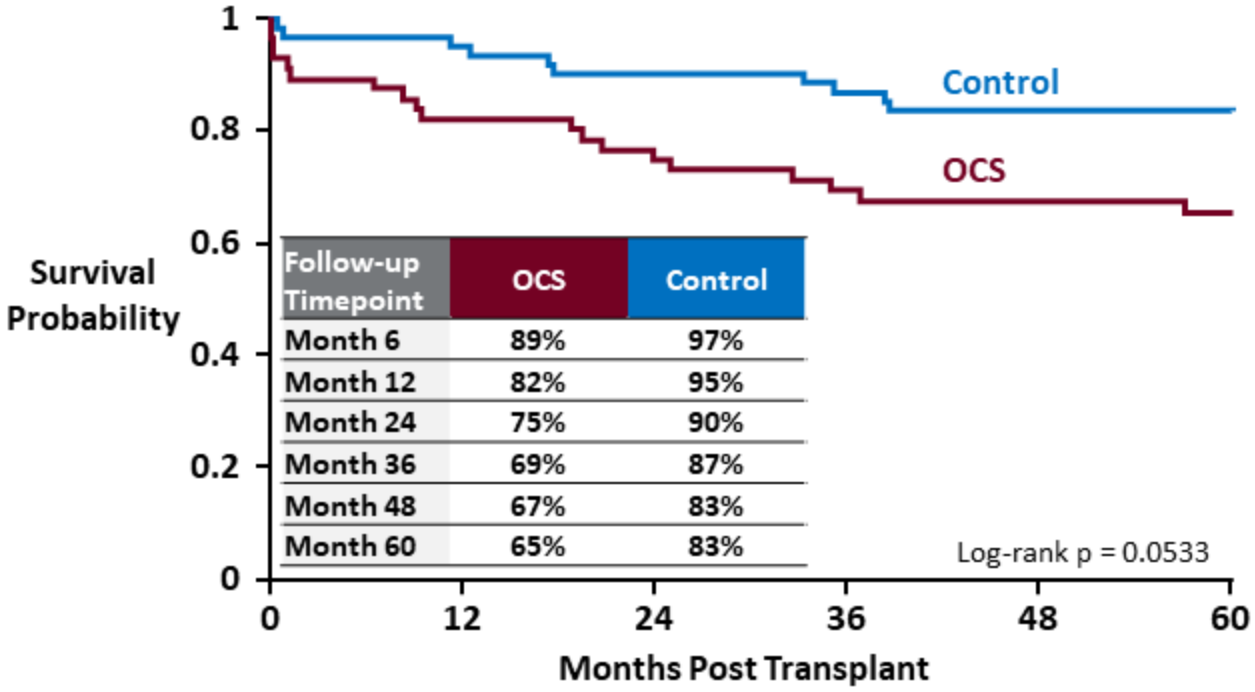


EXPAND and CAP Directly Support the Proposed Indication for Use, Not PROCEED II

1. Baran et al, Circ Heart Fail 2019

Post-Hoc Long-Term Survival Trend from UNOS Registry

Overall Survival

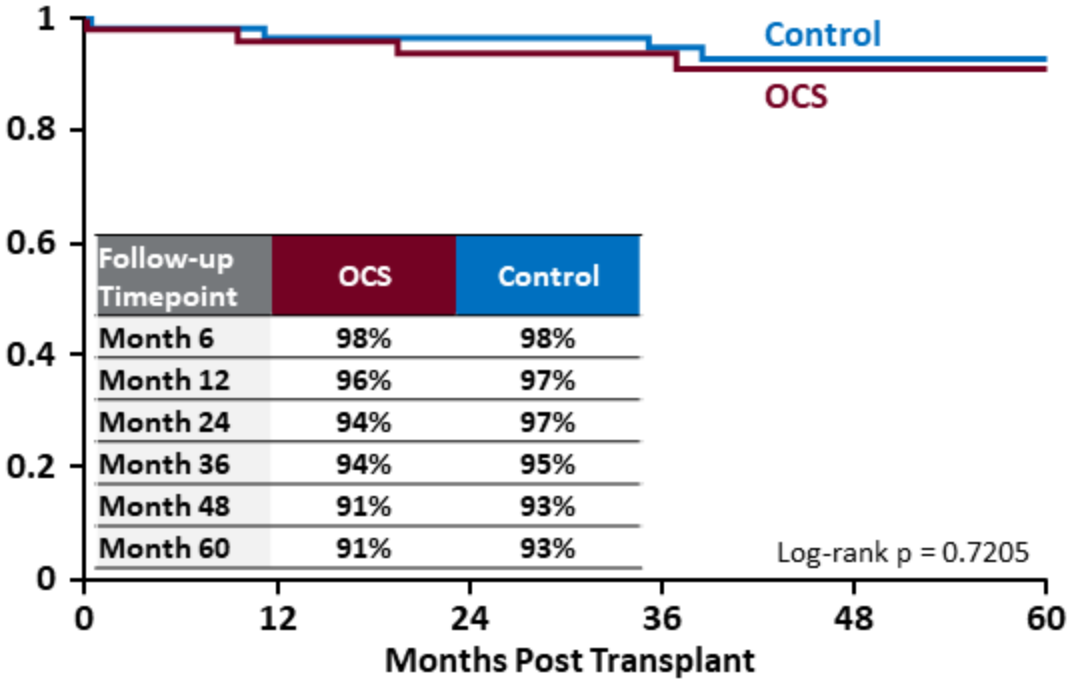


Follow-up Timepoint	OCS	Control
Month 6	89%	97%
Month 12	82%	95%
Month 24	75%	90%
Month 36	69%	87%
Month 48	67%	83%
Month 60	65%	83%

Log-rank p = 0.0533

Month	0	6	12	24	36	48	60
OCS	56	49	45	41	36	33	32
Control	62	59	58	54	51	48	48

Cardiac-related Survival

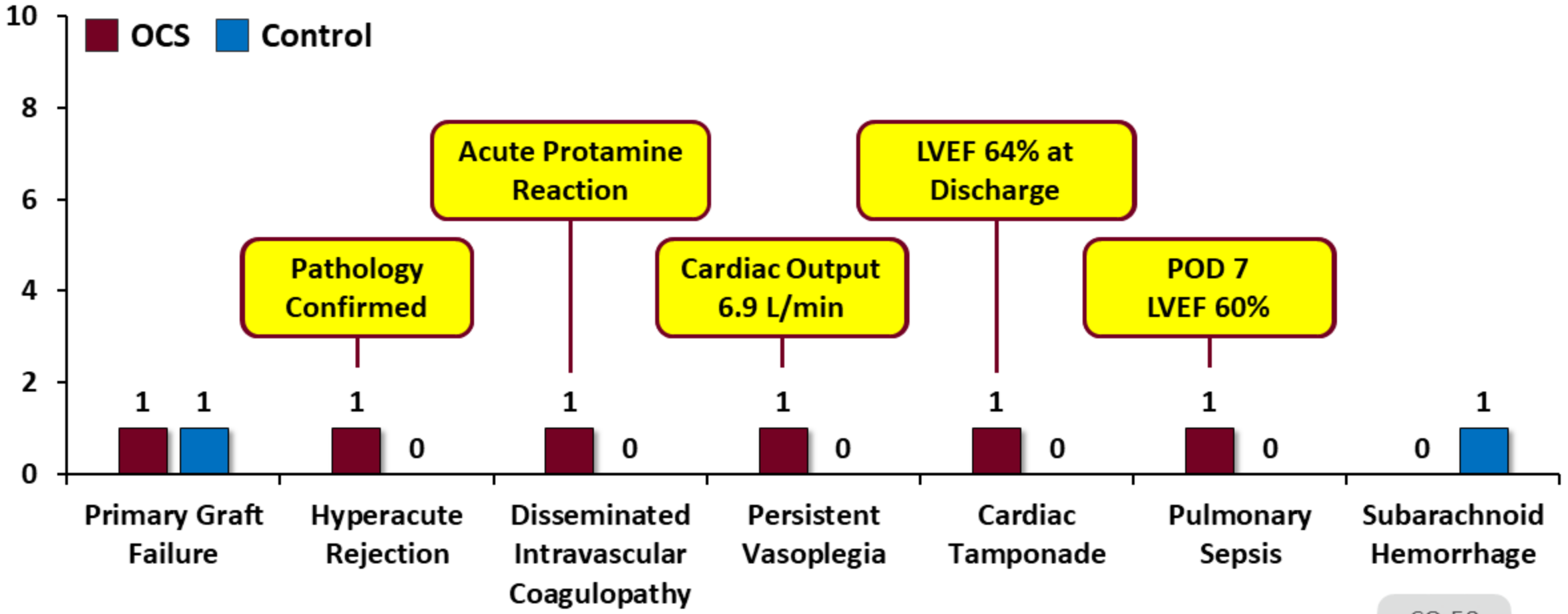


Follow-up Timepoint	OCS	Control
Month 6	98%	98%
Month 12	96%	97%
Month 24	94%	97%
Month 36	94%	95%
Month 48	91%	93%
Month 60	91%	93%

Log-rank p = 0.7205

0	6	12	24	36	48	60
56	49	45	41	36	33	32
62	59	58	54	51	48	48

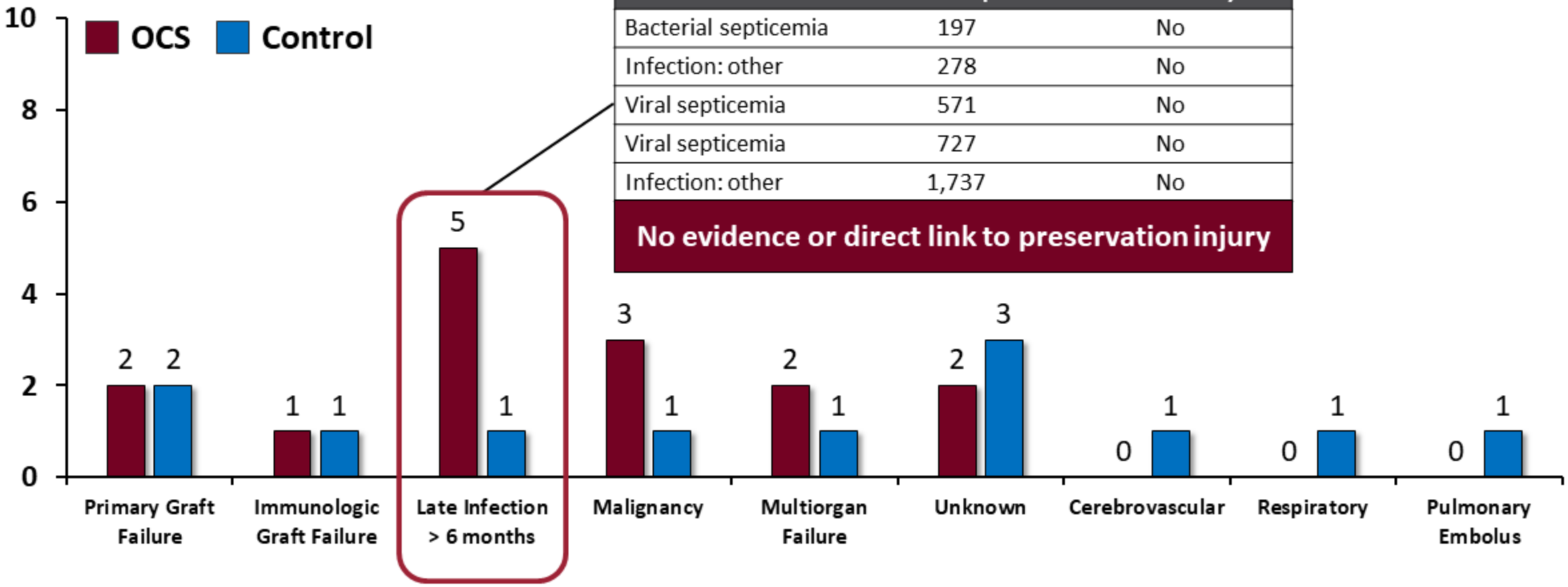
Causes of Mortality in PROCEED II Trial ≤ 60 Days Post Transplant



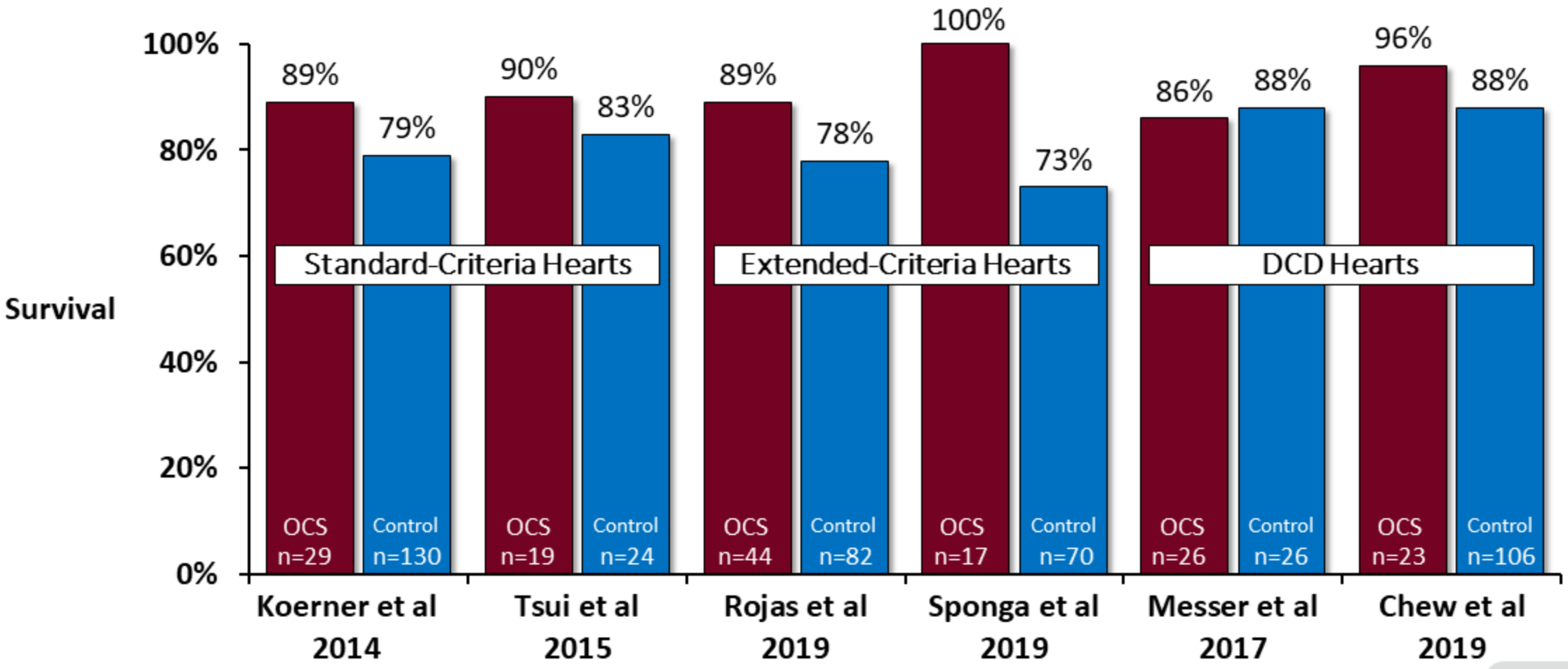
Causes of Mortality in PROCEED II Trial > 60 Days Post Transplant: UNOS Registry

Cause of Death	Death Days Post Transplant	Infection AE or SAE within 30 Days
Bacterial septicemia	197	No
Infection: other	278	No
Viral septicemia	571	No
Viral septicemia	727	No
Infection: other	1,737	No

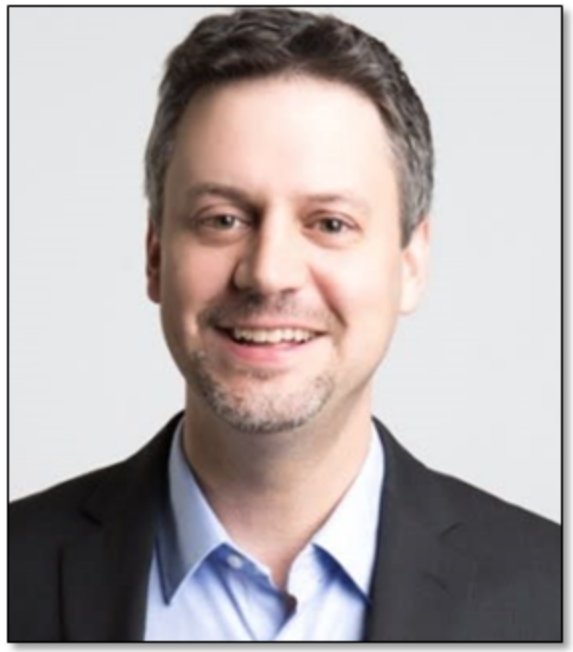
No evidence or direct link to preservation injury



Published International Studies Show Favorable OCS Long-Term Survival (N=165 OCS Cases)



TransMedics®



Statistical Considerations for Long-Term Survival

Chris Mullin, MS

Director, Product Development Strategy

NAMSA

Background on FDA Models to Extrapolate Long-Term Survival

- FDA developed model based on preliminary PROCEED II data (2015)
- FDA used this model to extrapolate long-term survival results in:
  - PROCEED II
  - EXPAND

Concerns About Underlying Assumptions of FDA Model

- Parametric models use strong assumptions for underlying hazard rates
- Specific concerns with piecewise-exponential model
  - Model choice and cut points all post hoc
  - Data-driven cut points can lead to bias / error inflation
- No clinical justification provided for cut points selected by FDA
  - Calls into question validity of model

FDA Model Underestimates Long-Term Survival

Time Post Transplantation	Difference Between Kaplan-Meier and Piecewise Exponential Survival Estimates (Percentage Points)		
	PROCEED II OCS Heart	PROCEED II SOC	EXPAND OCS Heart
1 Year	1.0	0.1	0.0
2 Years	0.3	1.0	-0.1
3 Years	1.1	-1.4	0.3
4 Years	-1.4	-3.2	?
5 Years	-3.5	-8.3	?

Source: FDA Executive Summary, Table 23 – Estimated Survival Probability PROCEED II and Table 41 – Survival Probability EXPAND

Summary of Concerns About FDA's Model to Extrapolate Long-Term Survival

- Choice of model for extrapolation is questionable
- FDA's model is inaccurate at predicting long-term survival
- Results show FDA's model appears neither valid nor reliable for extrapolation of long-term data in heart transplantation

TransMedics

TransMedics Positions On FDA Questions

Waleed Hassanein, MD
President and CEO
TransMedics

Question 1: EXPAND Design & Conduct

EXPAND is Well Designed, Clinically and Statistically Robust. UNOS Registry Data Analysis Validated the Inclusion Criteria of Extended-Criteria Donor Hearts in the U.S.

Study Design

- Randomization of extended-criteria hearts to cold storage **is not ethical**
- Concurrent controls **could be obtained from UNOS database for U.S. transplants**
- PG predicated on observed success rate of **80%**
- Donor heart inclusion criteria **independently defined by experts and proven to be significantly different than standard U.S. heart transplants based on UNOS database analysis**

Question 1: EXPAND Design & Conduct

The EXPAND & CAP Trial Were Conducted According to Highest Clinical Standards and the Adjudication Process Strictly Adhered to Trial Protocol

Trial Conduct

- **There were no revisions to donor heart inclusion criteria** – additional criteria recorded in original source documents were retabulated to provide the complete picture of risk factors in EXPAND donor population
- **There were no changes to severe PGD definition** – Medical Monitor consistently and strictly followed ISHLT criteria throughout adjudication
- **Sensitivity analysis demonstrated robustness of the endpoint regardless of adjudication**

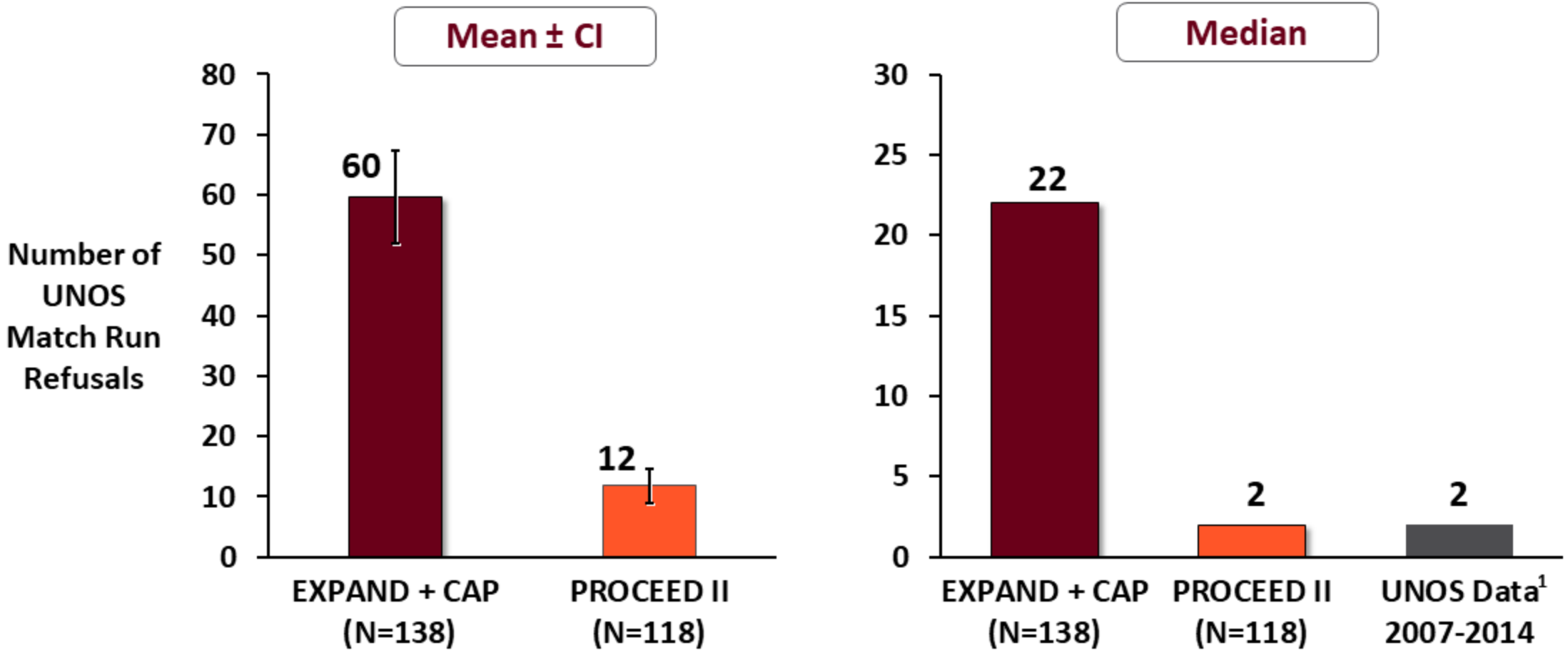
Question 2: EXPAND Inclusion Criteria

EXPAND & CAP Enrolled Donor Hearts That Are Seldomly Used for Transplants in the U.S. Based on UNOS Data Analysis

Donor Characteristics	EXPAND + CAP (N=138)	UNOS/SRTR* (N=10,873)	p-value
Age (years) – mean ± SD	36.4 ± 12.1	32.1 ± 11.0	< 0.0001
Age ≥ 55 years	13 (9%)	309 (3%)	0.0002
LVH >12 ≤ 16 mm	18 (19%)	Not collected	
Cross-clamp time ≥ 4 hours (Expected)	66 (48%)	1730 (16%)	< 0.0001
Cross-clamp time ≥ 4 hours (Actual)	113 (97%)	1730 (16%)	< 0.0001
LVEF between 40% - 50%	30 (22%)	500 (5%)	< 0.0001
Downtime ≥ 20 minutes	43 (31%)	255 (2%)	< 0.0001
Cross-clamp ≥ 4 hours plus ≥ 1 risk factor	23 (17%)	500 (5%)	< 0.0001
Downtime ≥ 20 minutes plus ≥ 1 risk factor	10 (7%)	61 (1%)	< 0.0001

*Data from 2015-2018 US Heart Transplant Registry

EXPAND Evaluated Donor Hearts That Are Not Routinely Transplanted in the US Today



1. Baran et al, Circ Heart Fail 2019

Question 3: Transplantability

Lactate Level and Trend Are Useful Guides to Managing Perfusion of Donor Hearts on OCS in Conjunction with AOP, CF and Overall Clinical Judgment

Prior clinical data have demonstrated that **lactate is a sensitive (63%) and highly specific (98%) biomarker for graft dysfunction**[1]

Lactate level/trend is **NOT** the only parameter or consideration for transplantabilty

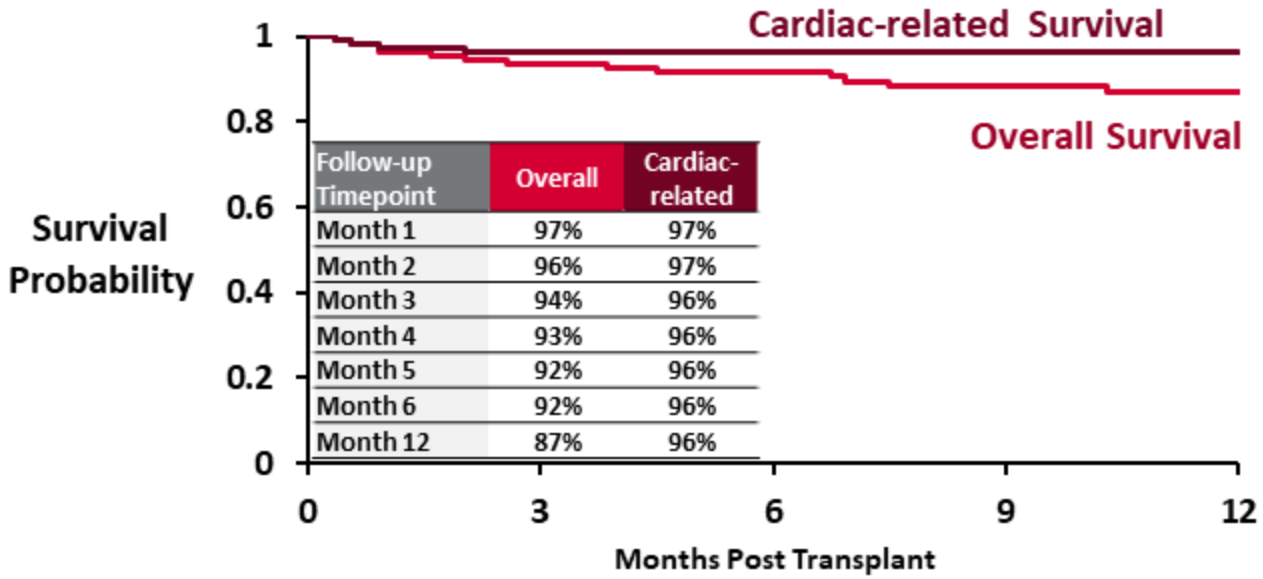
Used in conjunction with AOP, CF, and clinical judgment of the overall clinical test condition of the donor heart on OCS Heart System

This OCS Heart use model has been successfully used internationally with excellent clinical outcomes in DBD and DCD donor heart transplants

1. Hamed et al, JHLT 2009

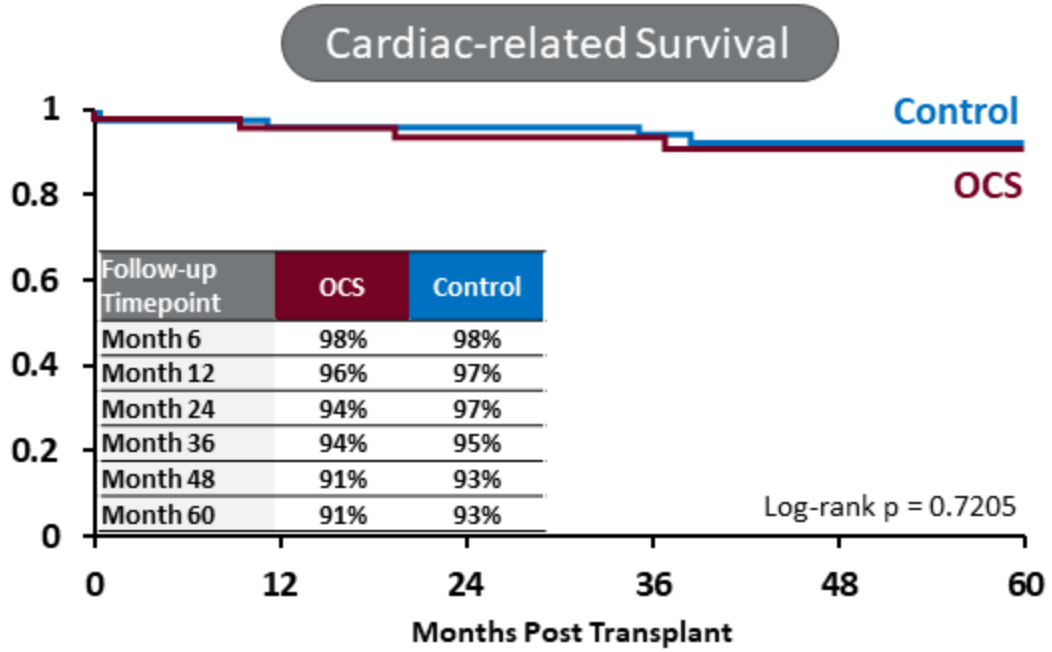
Question 4a & 4b: PROCEED II and EXPAND Study Analysis

Favorable Long-Term Survival for EXPAND + CAP Support the Approval of OCS for the Proposed Indication for Extended-Criteria Donor Hearts



Follow-up Timepoint	Overall	Cardiac-related
Month 1	97%	97%
Month 2	96%	97%
Month 3	94%	96%
Month 4	93%	96%
Month 5	92%	96%
Month 6	92%	96%
Month 12	87%	96%

EXPAND + CAP Trial Results



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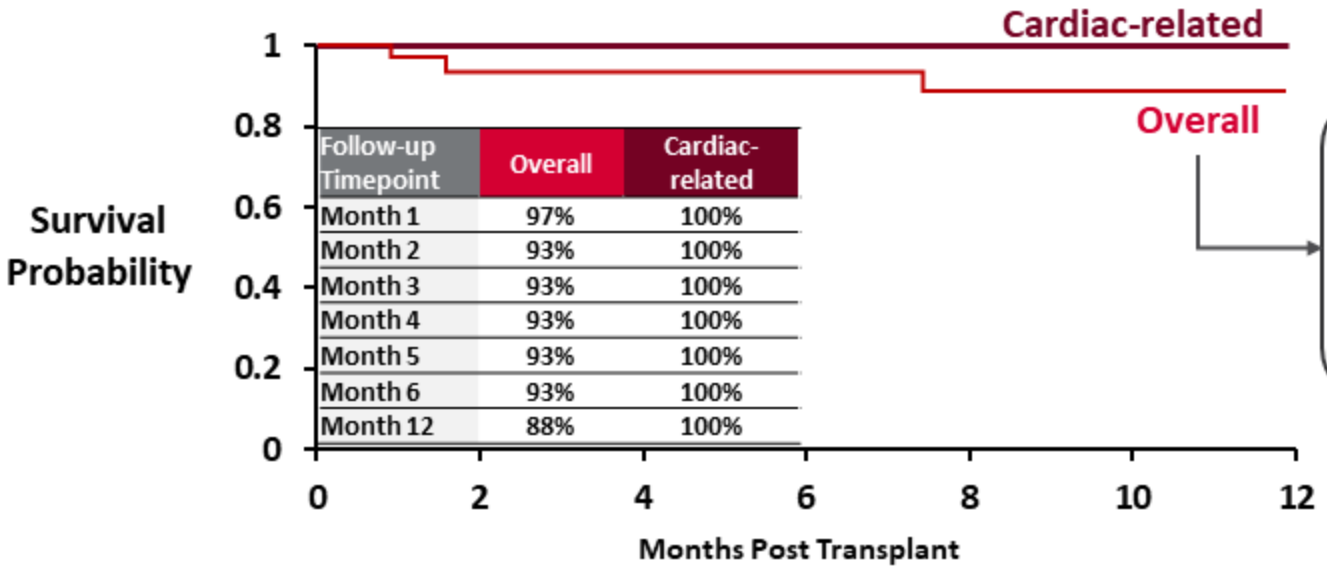
Month 36	94%	95%
Month 48	91%	93%
Month 60	91%	93%

PROCEED II Trial Results

Question 4c: Donor Hearts with ≥ 4 Hours Cross-Clamp Time

OCS Heart is Safe and Effective for Donor Hearts with ≥ 4 Hours of Expected Cross-Clamp Time

≥ 4-Hour Cross-clamp Criteria in EXPAND & CAP Population (N=33)



Follow-up Timepoint	Overall	Cardiac-related
Month 1	97%	100%
Month 2	93%	100%
Month 3	93%	100%
Month 4	93%	100%
Month 5	93%	100%
Month 6	93%	100%
Month 12	88%	100%

All 4 Deaths Were Not Cardiac-related

- Vasoplegia leading multiorgan failure
- Complications of pre-existing liver cirrhosis
- Non-recoverable CVA
- Motor vehicle accident (14 months)

Month	0	1	2	3	4	5	6	12
Overall	33	31	26	26	26	26	21	15
Cardiac-related	33	31	26	26	26	26	21	15

Question 5: Pathophysiology and Pathology

No Definitive Clinical Evidence of OCS-Related Injury of Donor Hearts. OCS Ability to Turn Down Potentially Bad Extended-Criteria Donor Hearts is a Clinical Benefit Not a Risk

- Donor hearts studied in EXPAND & CAP had significant risk factors making them highly unlikely to be used for transplantation – **many of these factors could contribute to pathological findings**
- **Brain death associated with significant physiologic changes** could show as pathological findings of a donor heart on histological examination of myocardium
- To our knowledge **there has never been any published or presented literature linking OCS Heart System to myocardial injury during perfusion**
- **84%** successful utilization of extended-criteria hearts is a significant clinical benefit

Question 6: Indications for Use

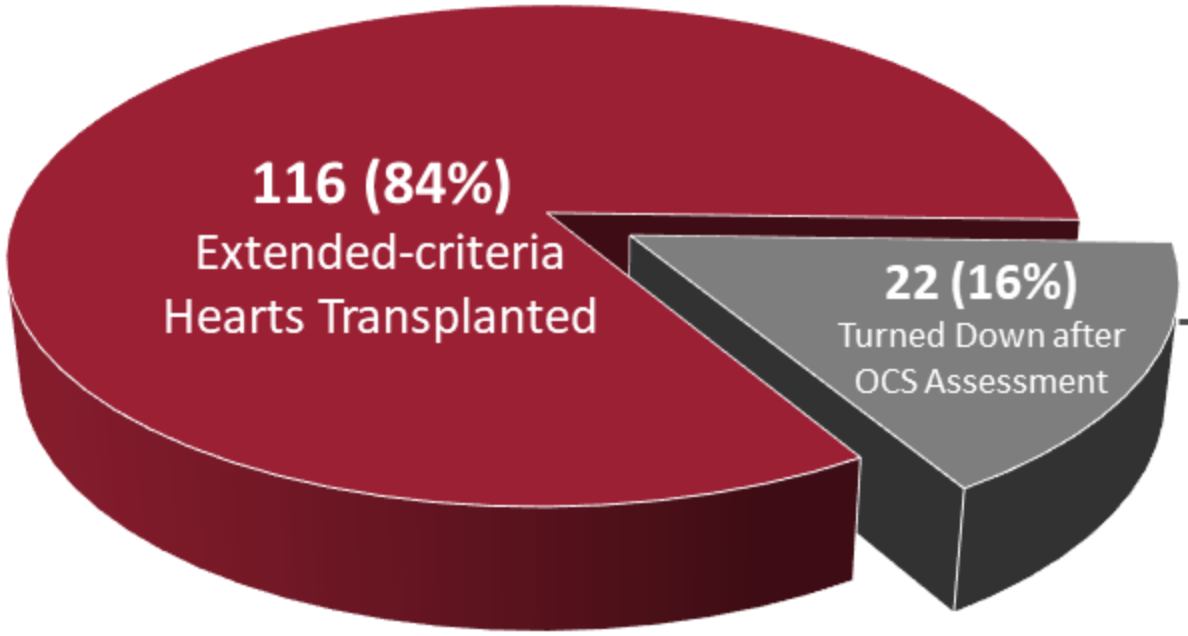
EXPAND & CAP Enrolled Donor Hearts That Are Seldomly Used for Transplants in the U.S. Based on UNOS Data Analysis and Match Run Refusals

The TransMedics® Organ Care System (OCS™) Heart System is a portable extracorporeal heart perfusion and monitoring system indicated for the resuscitation, preservation, and assessment of donor hearts intended for a potential transplant recipient in a near-physiologic, normothermic and beating state. OCS Heart is indicated for donor hearts with one or more of the following characteristics:

- Expected cross-clamp or ischemic time ≥ 4 hours due to donor or recipient characteristics (e.g., donor-recipient geographical distance, expected recipient surgical time); or
- Expected cross-clamp or ischemic time ≥ 2 hours AND one or more of the following:
  - Donor Age ≥ 55 years; or
  - Donors with history of cardiac arrest and downtime ≥ 20 minutes; or
  - Donor history of alcoholism; or
  - Donor history of diabetes; or
  - Donor Left Ventricle Ejection Fraction (LVEF) ≤ 50% but ≥ 40%; or
  - Donor history of Left Ventricular Hypertrophy (LVH) (septal or posterior wall thickness of > 12 ≤ 16 mm); or
  - Donor angiogram with luminal irregularities but no significant coronary artery disease (CAD)

Question 7: Benefit / Risk

84% Utilization of Extended-Criteria Donor Hearts Seldomly Used in the U.S. to Increase Heart Transplants Is a Significant Clinical and Public Health Benefit



Risk Profile of Turned-down Extended-criteria Hearts

- **72** mean match run refusals
- **55%** (12/22) had multiple donor heart risk factors

TransMedics

Training & Post-Approval Programs

Waleed Hassanein, MD
President and CEO
TransMedics

Dedicated Clinical Training Infrastructure

15,000 square-foot facility equipped with latest surgical and diagnostics equipment to replicate a retrieval environment

> 400 HCPs trained from 90 global academic and clinical institutions

Multi-Faceted Training Course

Classroom training for didactics and lessons learned

Demonstration and hands-on training for instrumentation and clinical management of the donor heart on OCS

Summary of OCS Heart Training Program

TRAINING

Initial hands-on clinical training and certification of every new clinical center starting OCS Heart program

SUPPORT

TransMedics provides 24/7 retrieval support via phone, messaging and email

TECHNOLOGY

Dedicated OCS Heart iPad® training and support application

Post Approval Program – FDA Question 8

New Enrollment Post-Approval Registry

- **175-patient**, single-arm, prospective post-approval registry
- Primary effectiveness endpoint: 12-month cardiac-related survival
  - PG of **86%**
  - Assumed success rate of **93%** required to meet the PG with 175 patients
- **12 months** of primary follow-up, then UNOS registry follow-up through 5 years

Continued Follow-up of EXPAND Patients

- UNOS registry follow-up of all EXPAND patients through 5 years
- Assess cardiac-related and all-cause survival

TransMedics

Clinical Perspective & Benefit-Risk Assessment

Ashish Shah, MD

Professor of Cardiac Surgery
Alfred Blalock Endowed Director and Chairman
Department of Cardiac Surgery

Vanderbilt University Medical Center

OCS Heart System Proposed Indication

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  - Donor history of Left Ventricular Hypertrophy (LVH) (septal or posterior wall thickness of > 12 ≤ 16 mm); or
  - Donor angiogram with luminal irregularities but no significant coronary artery disease (CAD)

EXPAND Targeted Donor Hearts Not Typically Used for Transplantation in the U.S.

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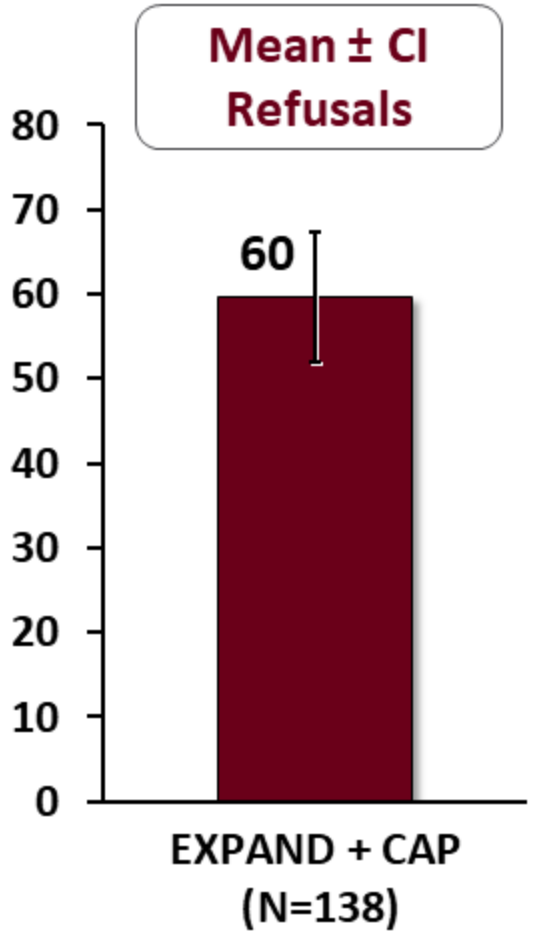
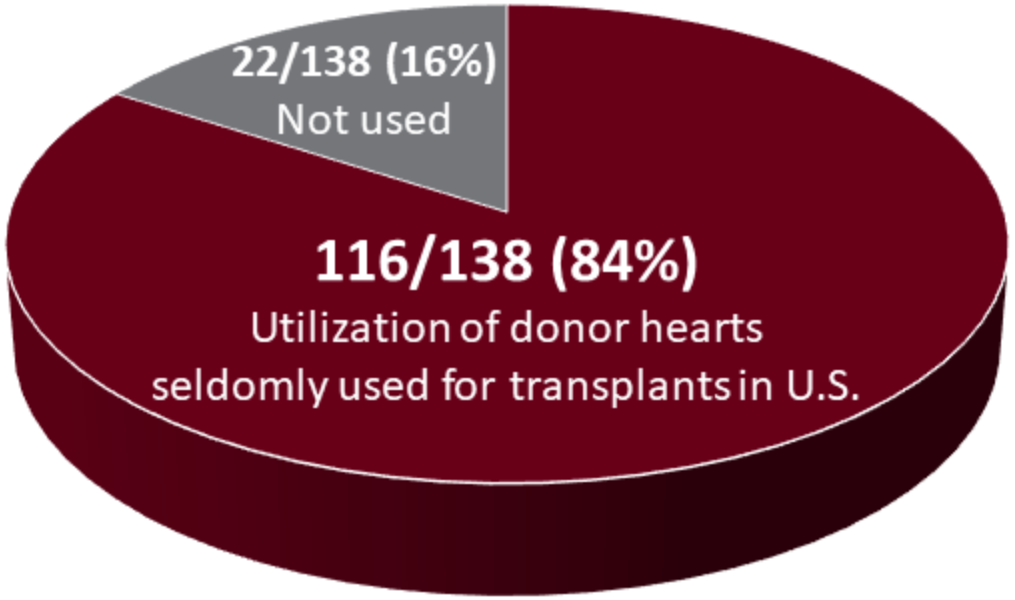


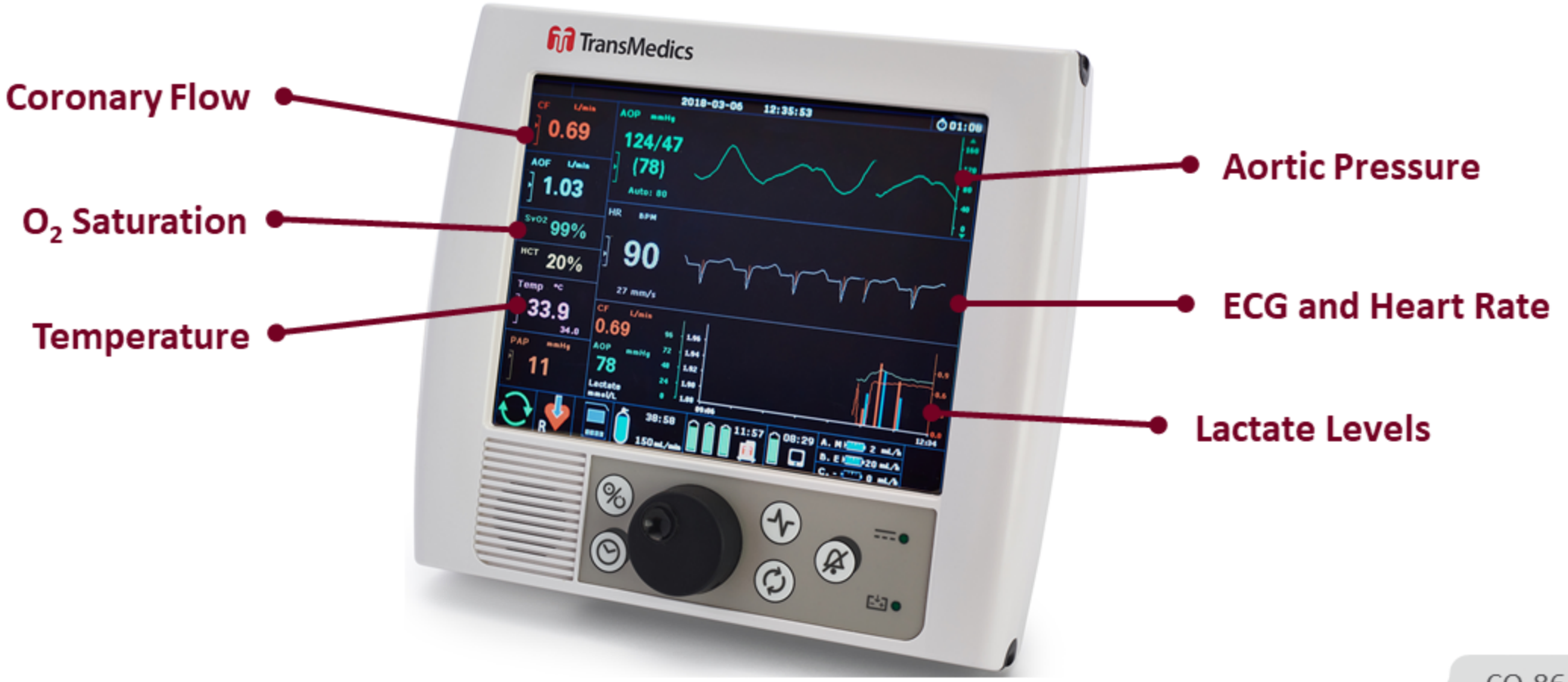
*Data from 2015-2018 US Heart Transplant Registry

Increased Donor Heart Utilization for Transplantation – Huge Clinical Benefit for Heart Failure Patients in U.S.

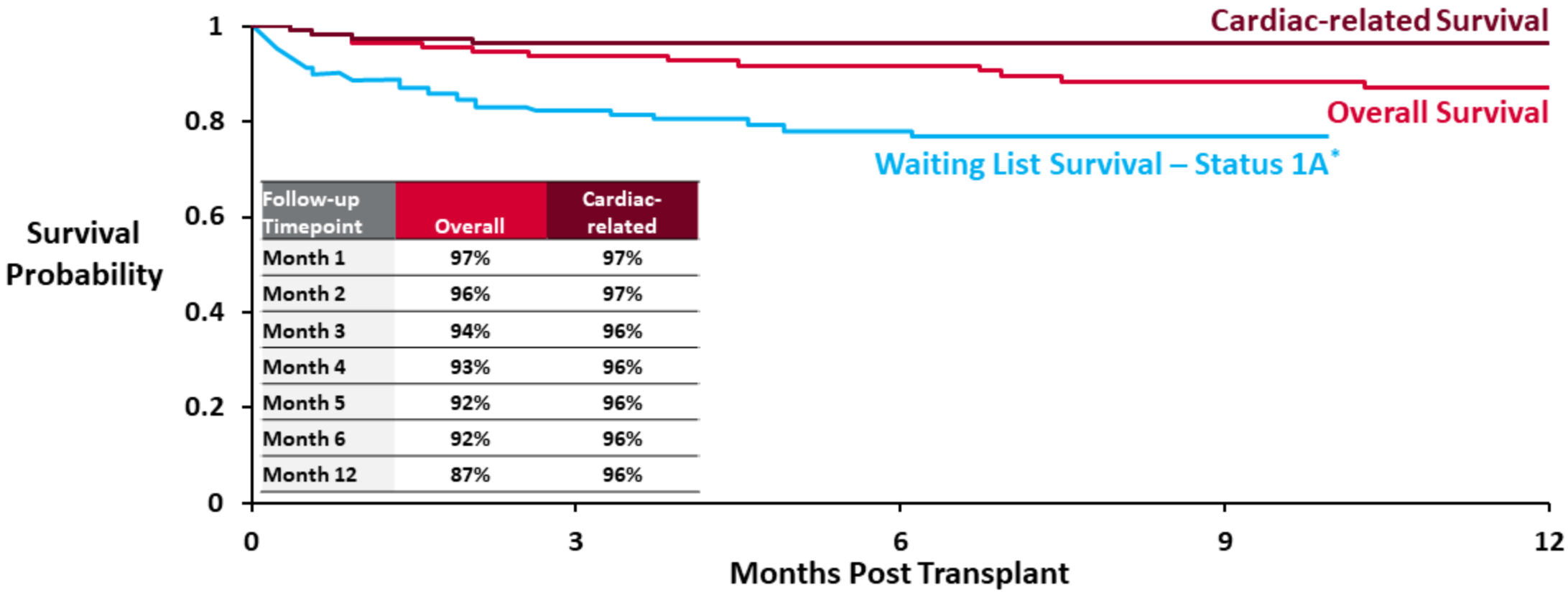


- This high rate of donor heart utilization could double the number of transplants
- Significant clinical and public health benefit to increase heart transplant procedures in the U.S.

OCS Provides Additional Data to Inform Clinical Decision-Making on Transplantability vs Flying Blind with Cold Storage



Favorable Long-Term Clinical Outcomes in EXPAND + CAP

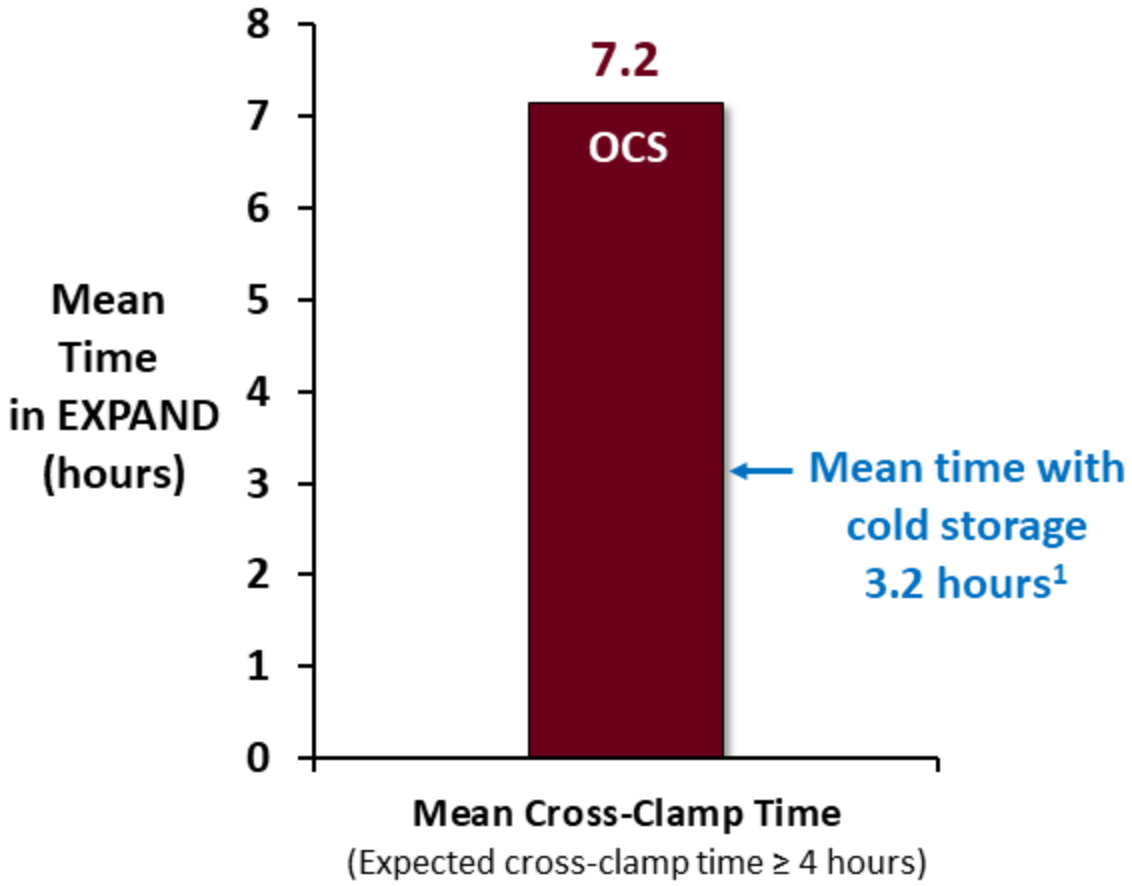


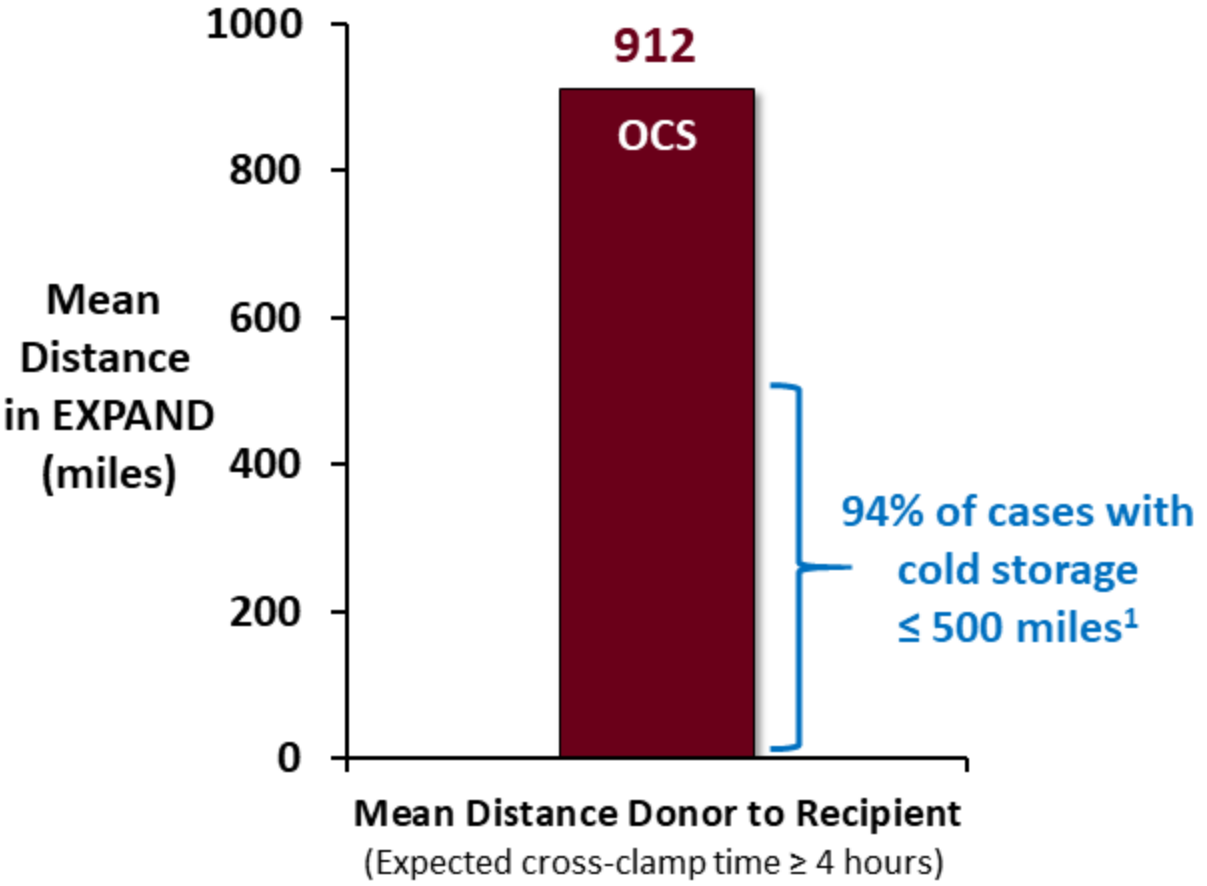
Follow-up Timepoint	Overall	Cardiac-related
Month 1	97%	97%
Month 2	96%	97%
Month 3	94%	96%
Month 4	93%	96%
Month 5	92%	96%
Month 6	92%	96%
Month 12	87%	96%

Month	0	1	2	3	4	5	6	12
Overall	116	111	100	98	97	96	85	65
Cardiac-related	116	111	100	98	97	96	85	65

*Stehlik et al, Circ Heart Fail 2017

OCS Heart Resulted in Distant Procurement of Donor Hearts That Could Not Be Achieved by Cold Storage





1. Baran et al, Circ Heart Fail 2019

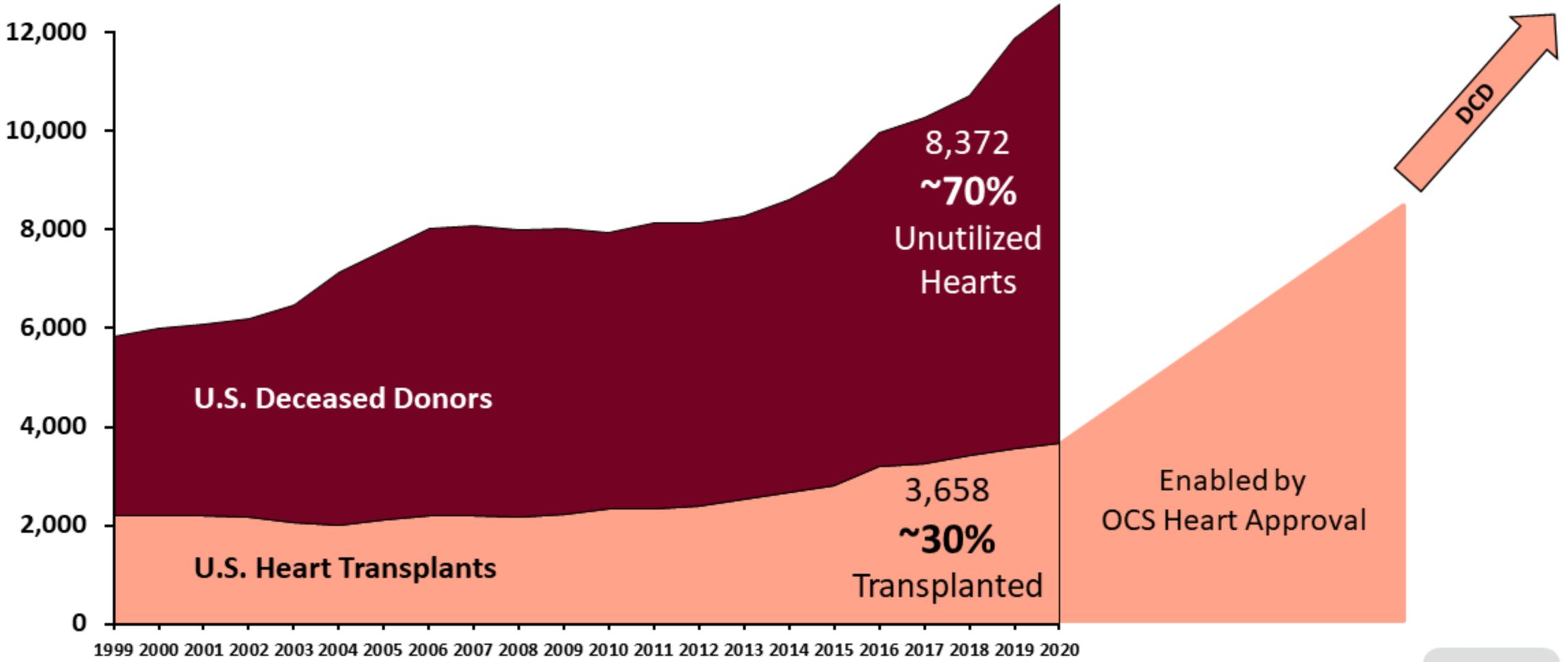
OCS May Enable National Sharing of Donor Hearts – Pushing Historical Boundaries of Cold Storage

*Recent case from EXPAND CAP. Data not yet submitted to the FDA.

OCS Heart Enables Use of Donor Hearts That Cannot Be Safely Preserved with Cold Storage

- 38-year-old donor who died from cerebrovascular hemorrhage
  - Distance from recipient hospital **> 1,000 miles**
  - Heart turned down **327 times** by other transplant centers before acceptance in EXPAND study
- 60+-year-old recipient with cardiomyopathy
  - Blood type O
  - Status 1A
  - On LVAD for ~1 year prior to transplant
- Patient transplanted, discharged within 2 weeks, doing well 4 years post transplant

What Approval of OCS Heart Could Mean for Heart Transplant in the United States



OCS™ Heart System for the Resuscitation, Preservation, and Assessment of Donor Hearts

April 6, 2021

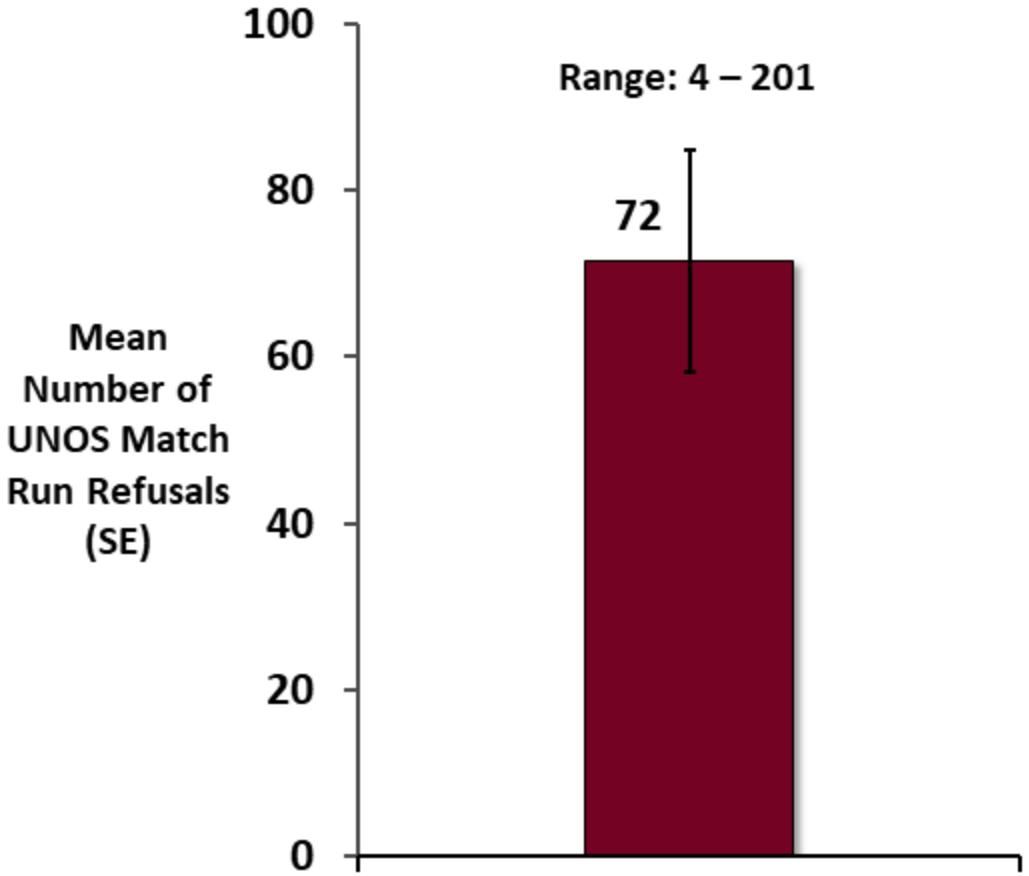
Circulatory System Devices Panel

TransMedics®

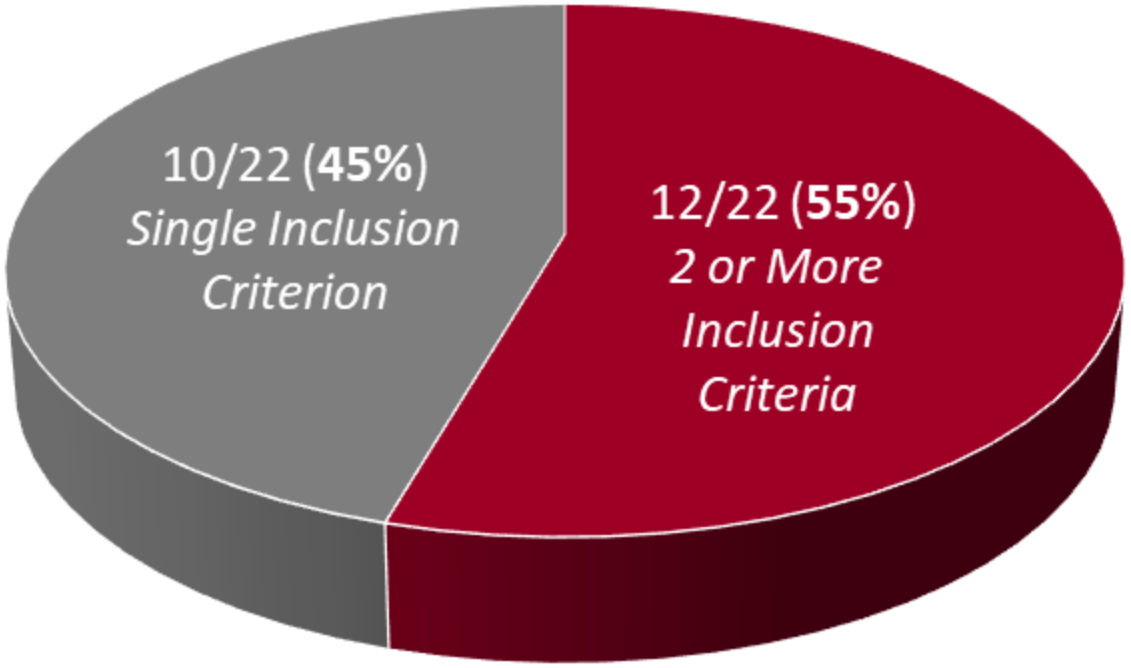
Back up Slides Shown

Profile of Turned Down Hearts in EXPAND + CAP

Match Run Refusals



Inclusion Criteria



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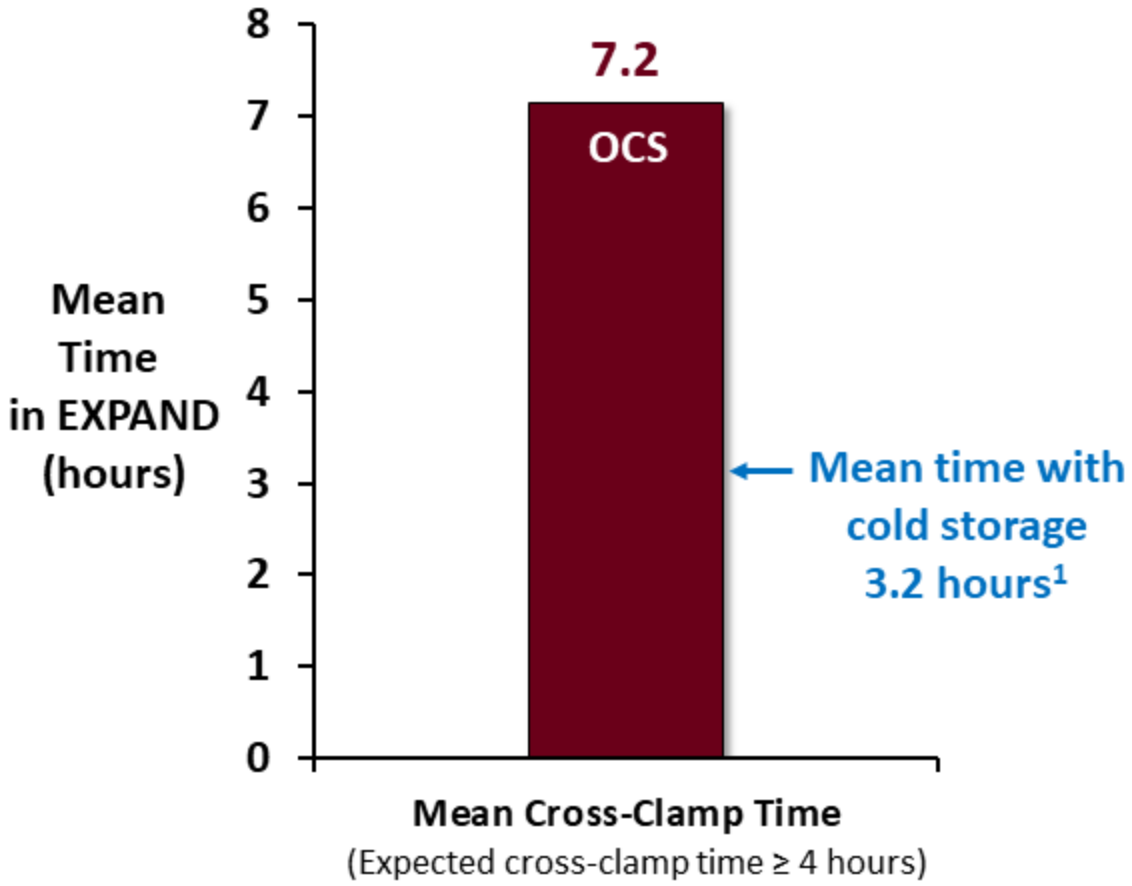
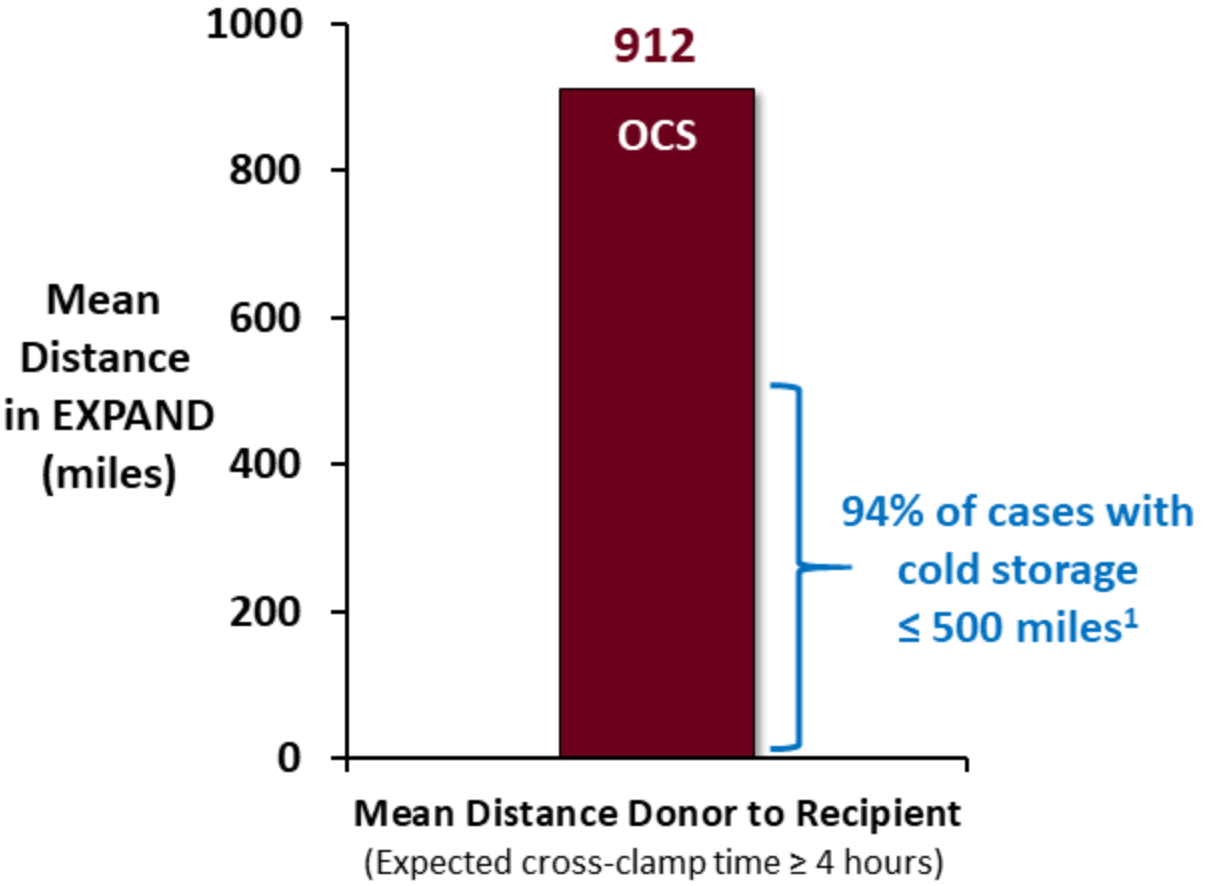
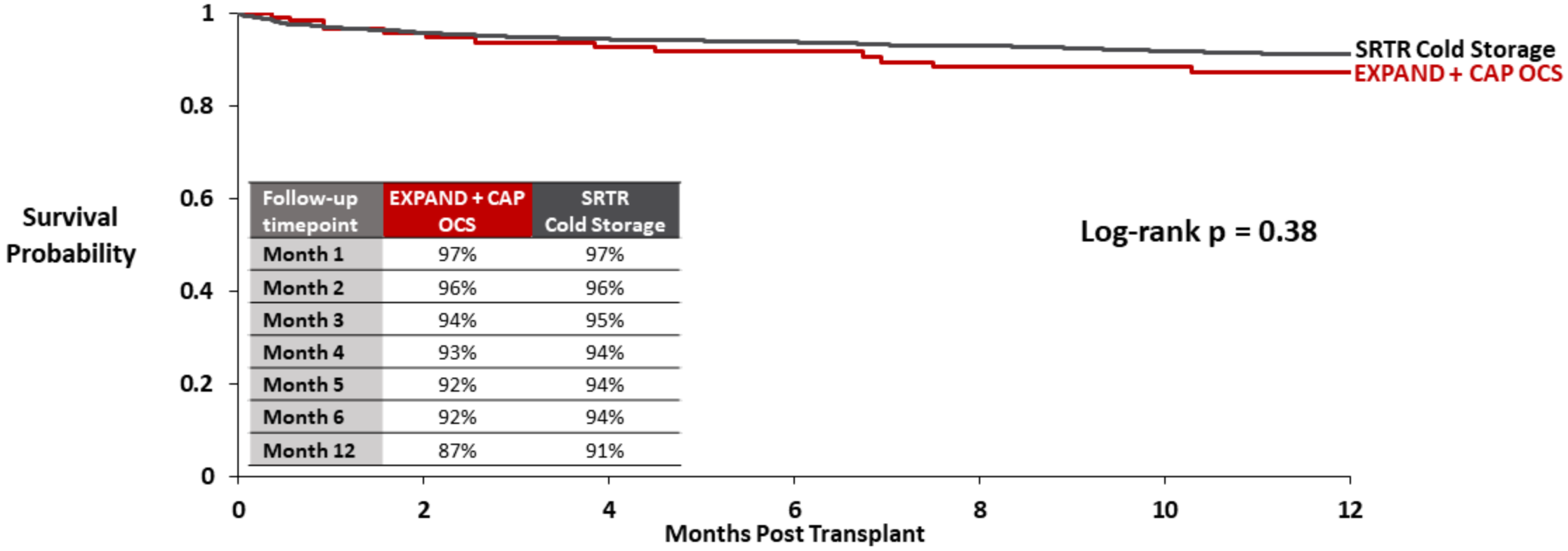




1. Baran et al, Circ Heart Fail 2019

Post-Hoc Analysis of Overall Survival in EXPAND + CAP vs SRTR Standard-Criteria Heart Transplant Recipients at Same Sites During Same Time Frame

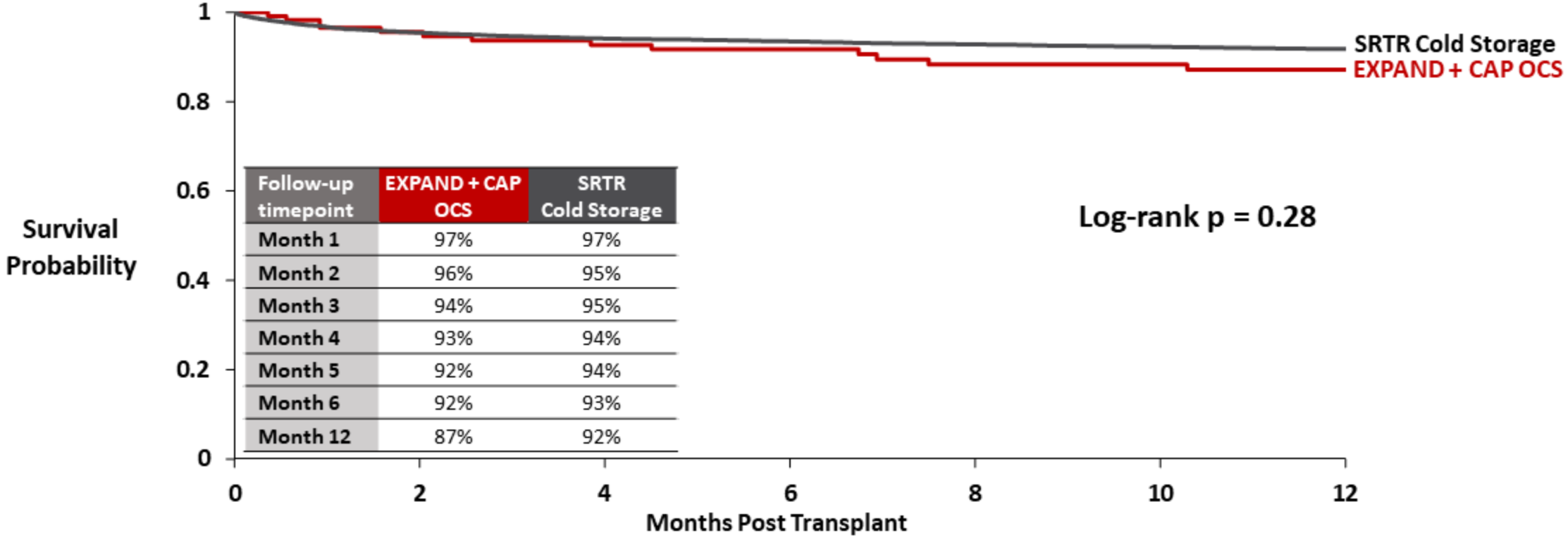


Follow-up timepoint	EXPAND + CAP OCS	SRTR Cold Storage
Month 1	97%	97%
Month 2	96%	96%
Month 3	94%	95%
Month 4	93%	94%
Month 5	92%	94%
Month 6	92%	94%
Month 12	87%	91%

Month	0	1	2	3	4	5	6	12
EXPAND + CAP OCS	116	111	100	98	97	96	85	65
SRTR Cold Storage	1,813	1,752	1,724	1,707	1,695	1,687	1,626	1,284

Analysis for Panel Questions – Not reviewed by FDA

Post-Hoc Analysis of Overall Survival in EXPAND + CAP vs SRTR Standard-Criteria Heart Transplant Recipients During Same Time Frame



Follow-up timepoint	EXPAND + CAP OCS	SRTR Cold Storage
Month 1	97%	97%
Month 2	96%	95%
Month 3	94%	95%
Month 4	93%	94%
Month 5	92%	94%
Month 6	92%	93%
Month 12	87%	92%

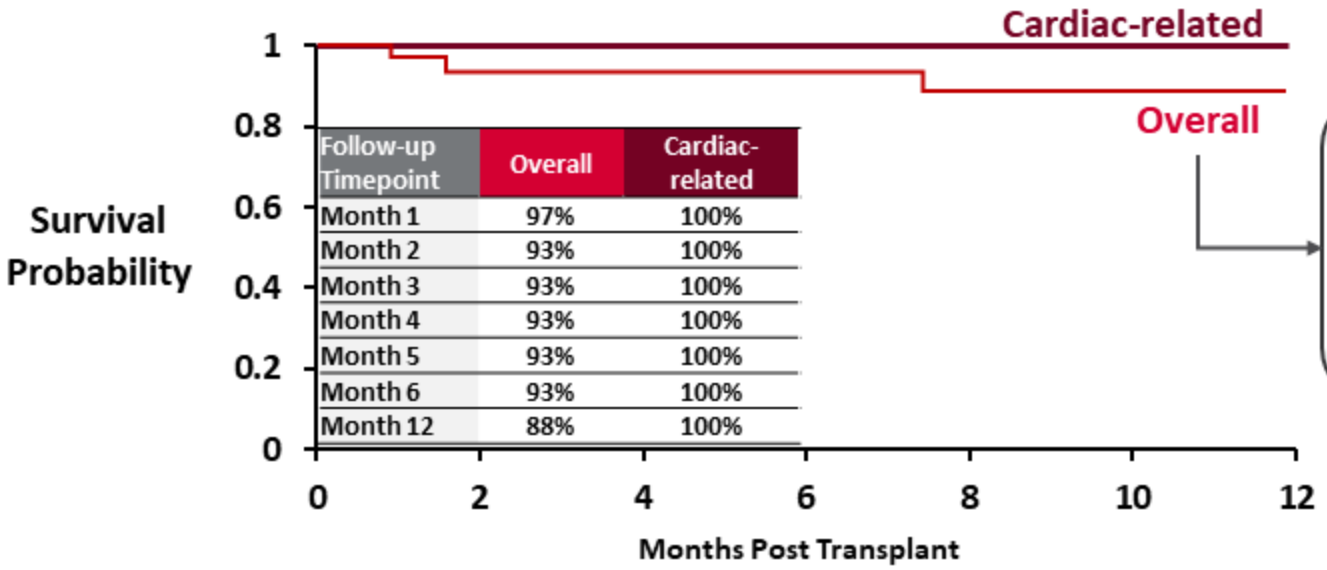
Month	0	1	2	3	4	5	6	12
EXPAND + CAP OCS	116	111	100	98	97	96	85	65
SRTR Cold Storage	10,873	10,484	10,330	10,240	10,172	10,116	9,689	7,855

Analysis for Panel Questions – Not reviewed by FDA

Question 4c: Donor Hearts with ≥ 4 Hours Cross-Clamp Time

OCS Heart is Safe and Effective for Donor Hearts with ≥ 4 Hours of Expected Cross-Clamp Time

≥ 4-Hour Cross-clamp Criteria in EXPAND & CAP Population (N=33)



Follow-up Timepoint	Overall	Cardiac-related
Month 1	97%	100%
Month 2	93%	100%
Month 3	93%	100%
Month 4	93%	100%
Month 5	93%	100%
Month 6	93%	100%
Month 12	88%	100%

All 4 Deaths Were Not Cardiac-related

- Vasoplegia leading multiorgan failure
- Complications of pre-existing liver cirrhosis
- Non-recoverable CVA
- Motor vehicle accident (14 months)

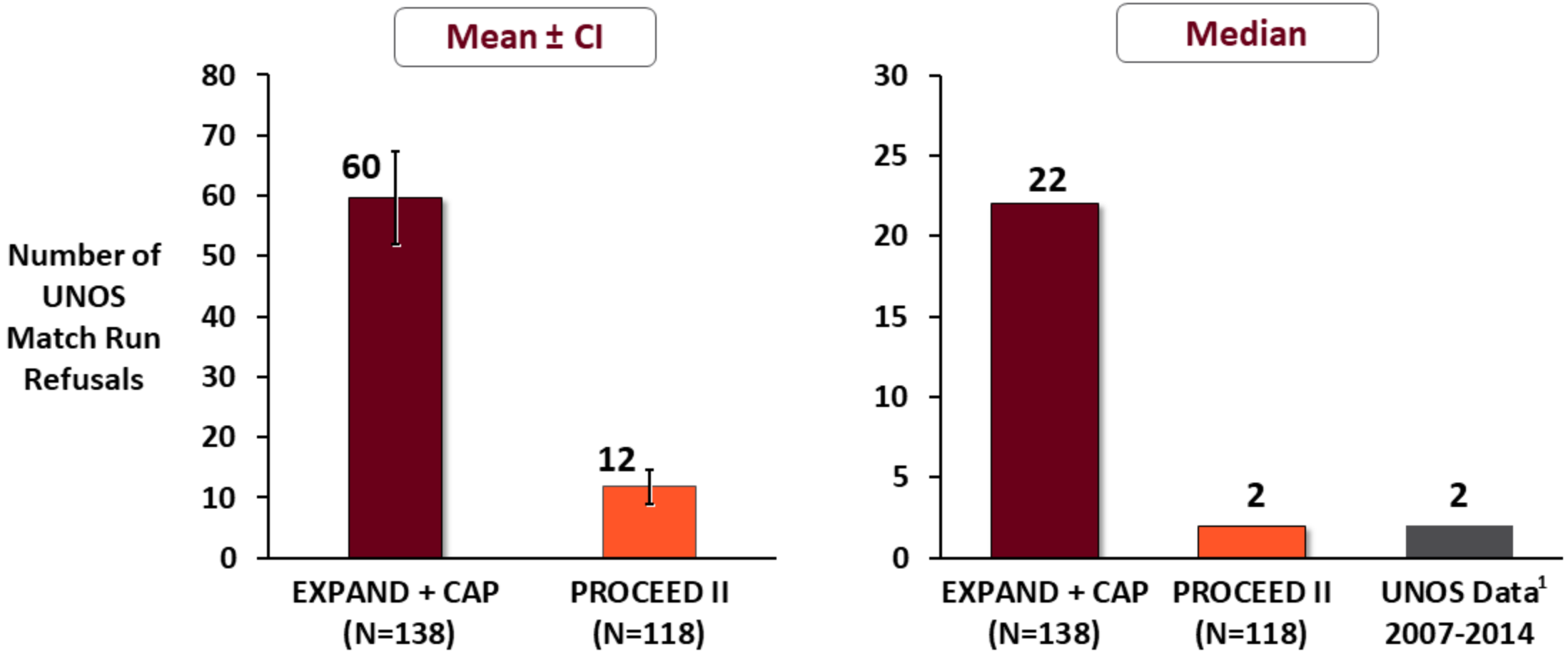
Month	0	1	2	3	4	5	6	12
Overall	33	31	26	26	26	26	21	15
Cardiac-related	33	31	26	26	26	26	21	15

Data are Poolable: Similar Primary Effectiveness Endpoint Results Across Sites

Site	Primary Effectiveness Endpoint	
	n/N	%
Overall	106/116	**91**
C-12	2/2	**100**
06/C-01	48/53	**91**
08	1/1	**100**
09	7/7	**100**
C-05	4/4	**100**
10	10/12	**83**
02	7/7	**100**
C-03	5/5	**100**
04	1/1	**100**
05	1/2	**50**
03/C-11	12/14	**86**
C-06	8/8	**100**

P-value for heterogeneity across sites = 0.91
(sites with < 5 patients pooled)

EXPAND Evaluated Donor Hearts That Are Not Routinely Transplanted in the US Today



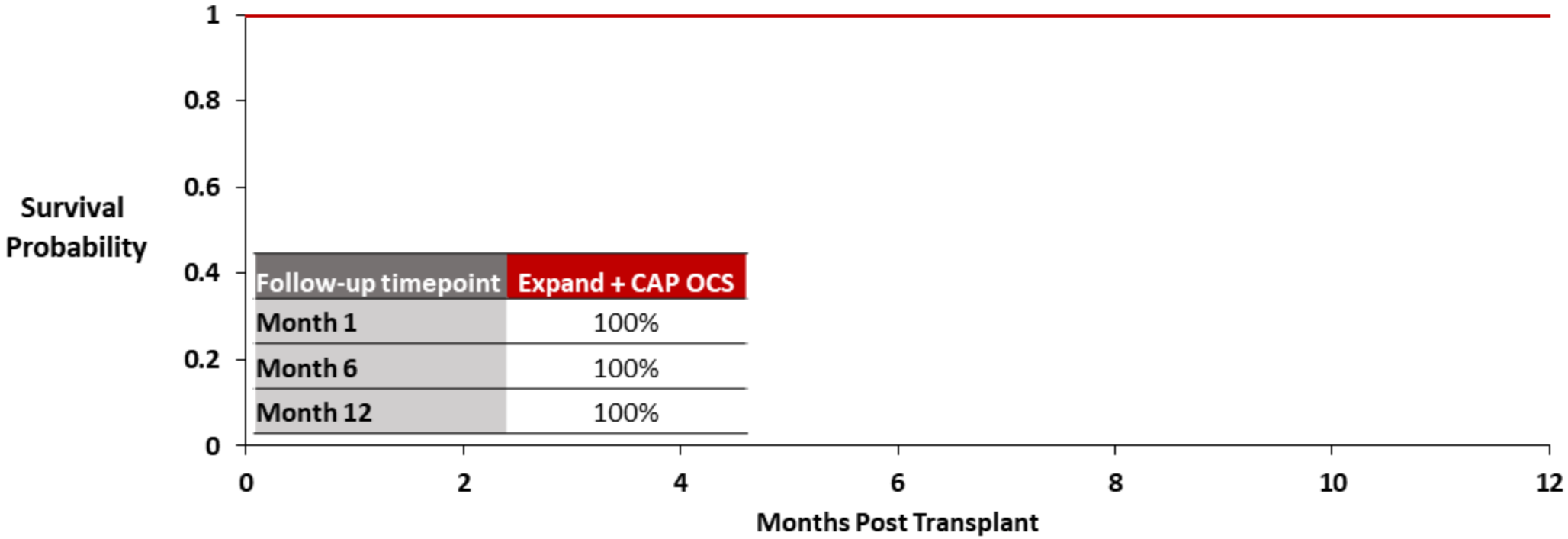
1. Baran et al, Circ Heart Fail 2019

Proposed Indication for Use Consistent with Study Criteria

The TransMedics® Organ Care System (OCS™) Heart System is a portable extracorporeal heart perfusion and monitoring system indicated for the resuscitation, preservation, and assessment of donor hearts intended for a potential transplant recipient in a near-physiologic, normothermic and beating state. OCS Heart is indicated for donor hearts with one or more of the following characteristics:

- Expected cross-clamp or ischemic time ≥ 4 hours due to donor or recipient characteristics (e.g., donor-recipient geographical distance, expected recipient surgical time); or
- Expected cross-clamp or ischemic time ≥ 2 hours AND one or more of the following:
  - Donor Age ≥ 55 years; or
  - Donors with history of cardiac arrest and downtime ≥ 20 minutes; or
  - Donor history of alcoholism; or
  - Donor history of diabetes; or
  - Donor Left Ventricle Ejection Fraction (LVEF) ≤ 50% but ≥ 40%; or
  - Donor history of Left Ventricular Hypertrophy (LVH) (septal or posterior wall thickness of > 12 ≤ 16 mm); or
  - Donor angiogram with luminal irregularities but no significant coronary artery disease (CAD)

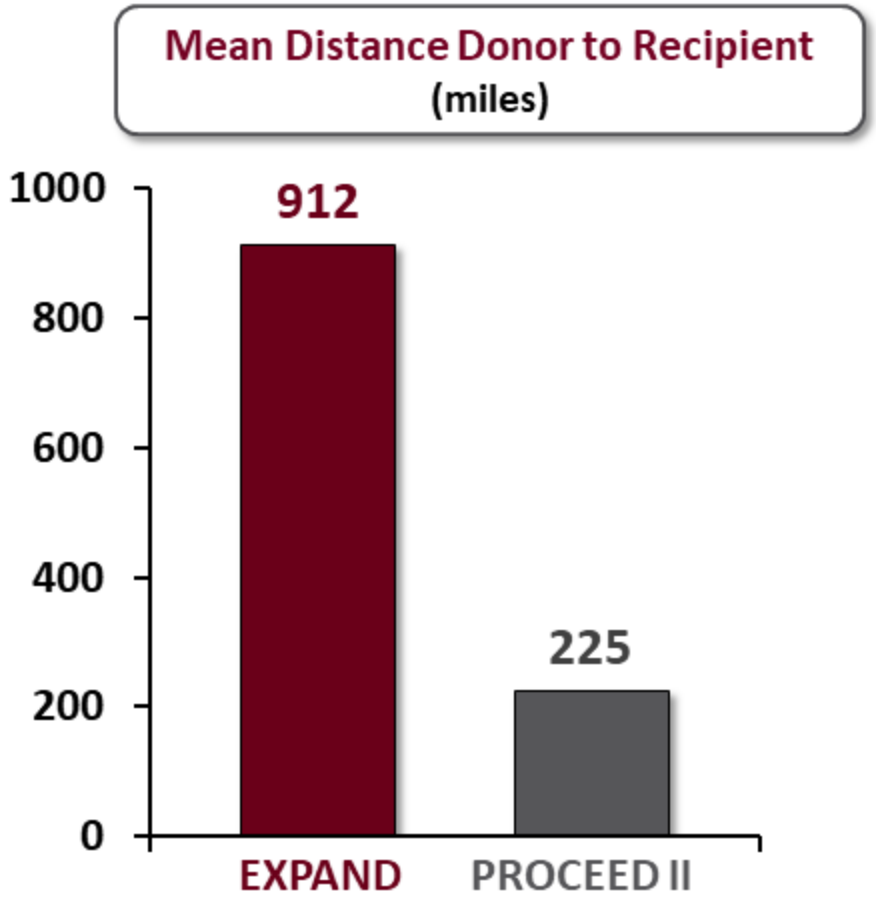
Kaplan-Meier Analysis of Overall Survival Expand + CAP OCS Patients with ≥ 4 hours of Ischemic Time and Any Additional Inclusion Criteria



Follow-up timepoint	Expand + CAP OCS
Month 1	100%
Month 6	100%
Month 12	100%

Month	0	1	6	12
Expand + CAP OCS	20	20	16	12

Geographic Distance Between Donor and Recipient Hospital for EXPAND and Proceed II



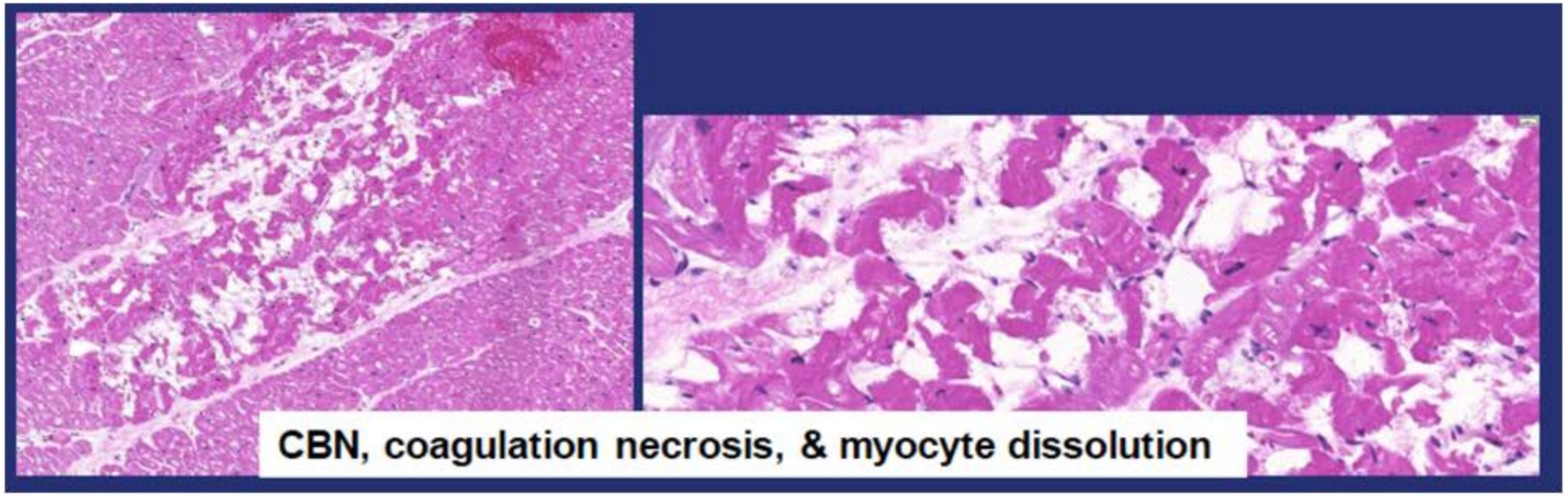
Conclusions from Histopathological Assessment of Turned-Down Donor Hearts in EXPAND

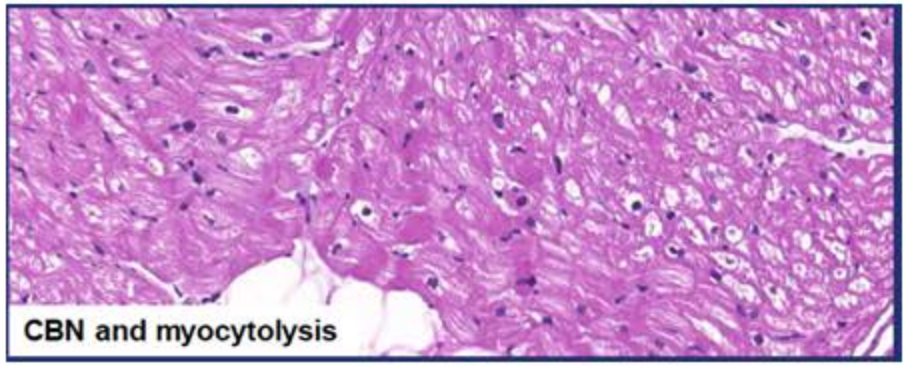
- Ischemia-reperfusion injury (IRI) is unavoidable ***regardless of preservation method***
- Most donor hearts already harbor some ischemic-type damage from peri-operative events[1,2]
  - Histopathological findings do not strongly correlate with function unless damage is extensive and heart is reperfused[1-2]
- Issue with cold storage: IRI is ***undetectable*** and is not observed ***until the donor heart is transplanted into the recipient***
- OCS offers benefit of allowing for proactive identification, monitoring, and responding to IRI *ex vivo* rather than reacting *in vivo* after transplant
  - Consistent with low rate of PGD in EXPAND and CAP vs literature rates with cold storage

No convincing evidence that OCS is "damaging" hearts – all observations consistent with IRI that would be present under any circumstances

1. Fyfe et al, Circulation 1996; 2. Nakamura et al, Cardiovasc Thoracic Surg 2019; 3. ISIS-2, J Am Coll Cardiol 1988.

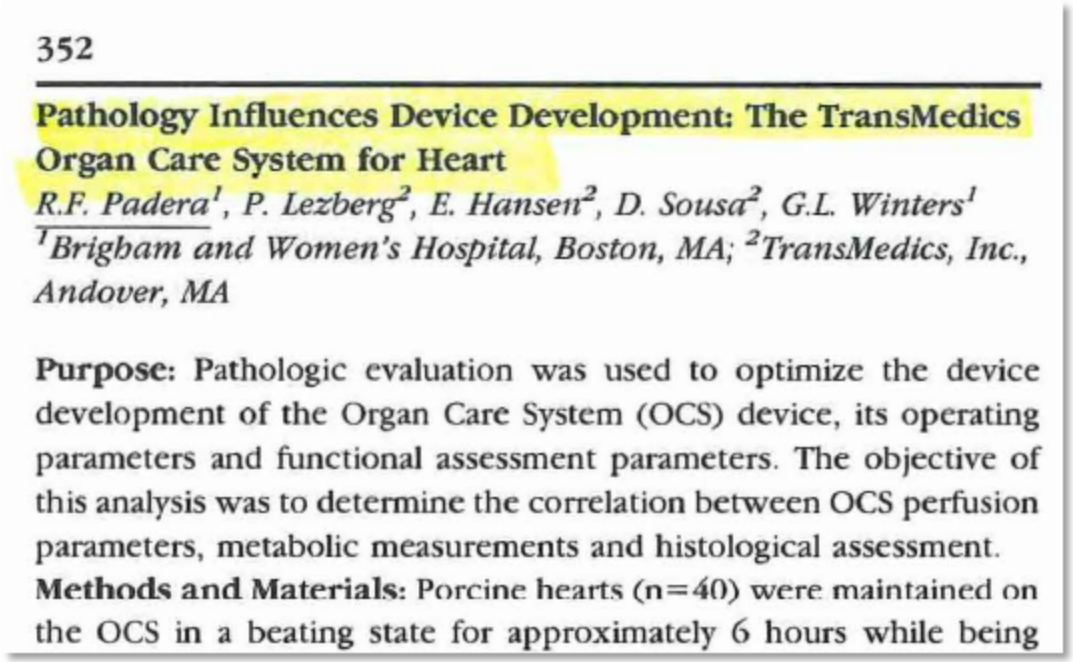
Observed Myocyte Dissolutions Take More Time to Develop than OCS Perfusion Times





Animal Study Pathological Evaluation of OCS Preserved Hearts

- (n=40) were maintained on the OCS in a beating state for approximately 6 hours while being perfused with warm oxygenated blood supplemented with the TransMedics Maintenance Solution.
- Microscopic sections were taken from the ventricles (8), atria (2) , pulmonary artery (I), aorta (I) and coronary arteries (2).
- Pathologists blinded to the experimental conditions, each slide was scored for ischemia, hemorrhage and edema on a scale from 0-4, and the scores for the ventricular slides.
- Pathologic evaluation validated the association of OCS enabled assessment parameters (CF, AOP, ending lactate levels) with ischemic damage.



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Pathology Influences Device Development: The TransMedics Organ Care System for Heart

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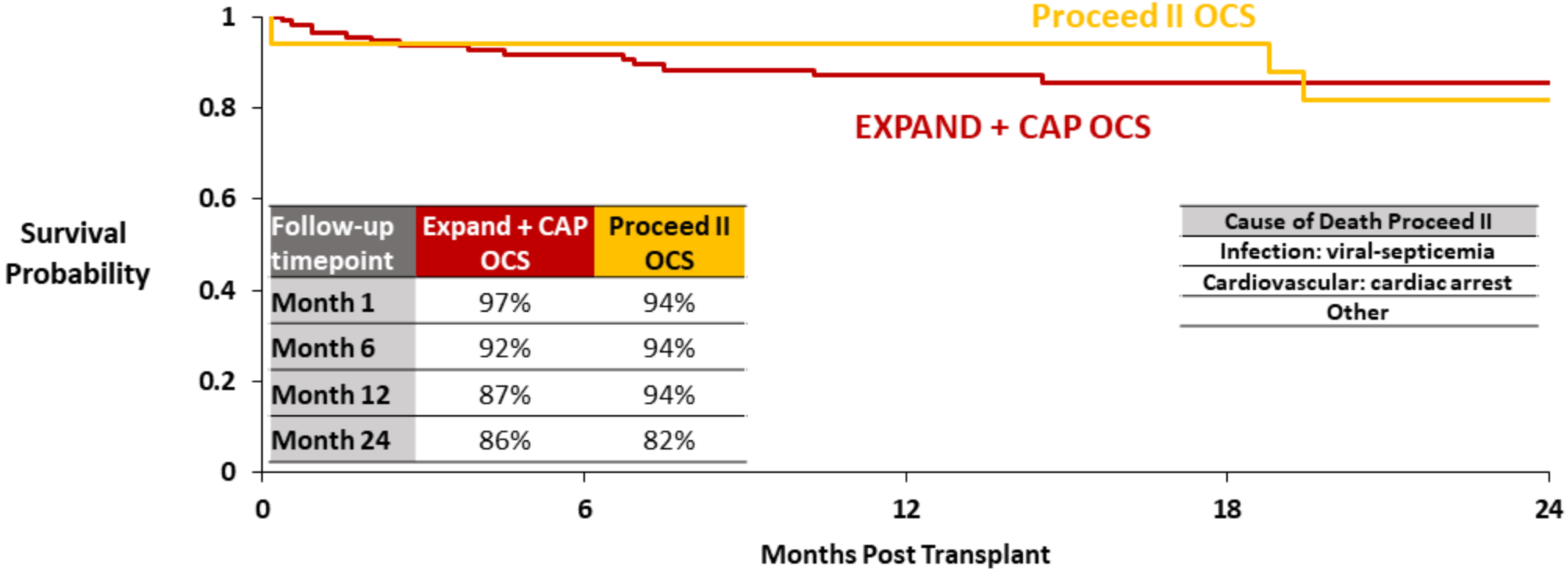
[1]Brigham and Women's Hospital, Boston, MA; [2]TransMedics, Inc., Andover, MA

Purpose: Pathologic evaluation was used to optimize the device development of the Organ Care System (OCS) device, its operating parameters and functional assessment parameters. The objective of this analysis was to determine the correlation between OCS perfusion parameters, metabolic measurements and histological assessment.
Methods and Materials: Porcine hearts (n=40) were maintained on the OCS in a beating state for approximately 6 hours while being

Kaplan-Meier Analysis of Overall Survival EXPAND + CAP OCS Patients vs. Proceed II Patients Who Met at Least One Expand Criteria



Follow-up timepoint	Expand + CAP OCS	Proceed II OCS
Month 1	97%	94%
Month 6	92%	94%
Month 12	87%	94%
Month 24	86%	82%

Cause of Death Proceed II
Infection: viral-septicemia
Cardiovascular: cardiac arrest
Other

Month	0	1	6	12	24
Expand + CAP OCS	116	111	85	65	30
Proceed II OCS	17	16	15	15	13

Mechanical Support Use in PROCEED II

	OCS (N=62)	Control (N=66)
Post-Transplant Mechanical Circulatory Support (MCS) – Any type (IABP, ECMO, VAD etc.)	**9 (14.5%)**	**7 (10.6%)**
IABP Only	3	5
VAD Only	0	1
ECMO Only	2	1
ECMO and IABP	1	0
VAD and IABP	2	0
VAD and ECMO	1	0
Patients with MCS + death within 30 days	**3***	**1#**
Patients who were discharged alive post MCS	**6 (9.7%)**	**6 (9.1%)**

*** OCS Deaths: 1 for PGD, 1 for Hyperacute Rejection and 1 for Acute Protamine Reaction**

 # Control Deaths: 1 for PGD