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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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SUPPLEMENTARY APPENDIX

Atrial Shunt Device for Heart Failure with Preserved and Mildly Reduced Ejection Fraction (REDUCE-LAP HF II): A Randomised, Multicentre, Blinded, Sham-Controlled Trial

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on behalf of the REDUCE LAP-HF-II investigators

CONTENTS

PARTICIPATING SITES AND COMMITTEES

Participating Sites and Investigators

Site number	Institution	Investigator	Principal investigator
0101	Northwestern University	James Flaherty	Yes
0101	Northwestern University	Laura Davidson	No
0101	Northwestern University	Benjamin Freed	No
0101	Northwestern University	Sadiya Khan	No
0101	Northwestern University	Jay Pandit	No
0101	Northwestern University	Sanjiv Shah	No
0102	Evanston Northshore Healthcare	Robert Gordon	Yes
0102	Evanston Northshore Healthcare	Marcela Goldsmith	No
0102	Evanston Northshore Healthcare	Charu Gupta	No
0102	Evanston Northshore Healthcare	Mark Lambert	No
0102	Evanston Northshore Healthcare	Justin Levisay	No
0102	Evanston Northshore Healthcare	David Marmor	No
0102	Evanston Northshore Healthcare	Mark Ricciardi	No
0102	Evanston Northshore Healthcare	Jonathan Rosenberg	No
0104	University of Arizona Medical Center University Campus	Elizabeth Juneman	Yes
0104	University of Arizona Medical Center University Campus	Mark Friedman	No
0104	University of Arizona Medical Center University Campus	Mathew Hutchinson	No
0104	University of Arizona Medical Center University Campus	Michael Insel	No
0104	University of Arizona Medical Center University Campus	Peter Ott	No
0104	University of Arizona Medical Center University Campus	Franz Rischard	No
0104	University of Arizona Medical Center University Campus	Nancy Sweitzer	No
0104	University of Arizona Medical Center University Campus	Preethi William	No
0104	University of Arizona Medical Center University Campus	Aaron Wolfson	No
0105	Massachusetts General Hospital	Gregory Lewis	Yes
0105	Massachusetts General Hospital	Sammy Elmariah	No
0105	Massachusetts General Hospital	Ignacio Inglessis	No
0105	Massachusetts General Hospital	Rajeev Malhotra	No
0108	Medical University of South Carolina	Sheldon Litwin	Yes
0108	Medical University of South Carolina	Brian Houston	No
0108	Medical University of South Carolina	Christopher Nielsen	No
0108	Medical University of South Carolina	Adrian Van Bakel	No
0108	Medical University of South Carolina	Michael Zile	No
0109	Vanderbilt University Medical Center	Deepak Gupta	Yes
0109	Vanderbilt University Medical Center	Evan Brittain	No

Site number	Institution	Investigator	Principal investigator
0109	Vanderbilt University Medical Center	Robert Piana	No
0109	Vanderbilt University Medical Center	Sharon Shen	No
0110	Wake Forest Health Sciences	Bharathi Upadhya	Yes
0110	Wake Forest Health Sciences	Thomas O'Neill	No
0110	Wake Forest Health Sciences	David Zhao	No
0111	Ohio State University Wexner Medical Center	Rami Kahwash	Yes
0111	Ohio State University Wexner Medical Center	Sitaramesh Emani	No
0111	Ohio State University Wexner Medical Center	Veronica Franco	No
0111	Ohio State University Wexner Medical Center	Garrie Haas	No
0111	Ohio State University Wexner Medical Center	Ayesha Hasan	No
0111	Ohio State University Wexner Medical Center	Brent Lampert	No
0111	Ohio State University Wexner Medical Center	Scott Lilly	No
0111	Ohio State University Wexner Medical Center	David Orsinellli	No
0111	Ohio State University Wexner Medical Center	Ajay Vallakati	No
0113	Ohio Health Research Institute	Anupam Basuray	Yes
0114	Mayo Clinic - Rochester	Barry Borlaug	Yes
0114	Mayo Clinic - Rochester	Omar Abou-Ezzeddine	No
0114	Mayo Clinic - Rochester	Alison Cabalka	No
0114	Mayo Clinic - Rochester	Michel Corban	No
0114	Mayo Clinic - Rochester	Christopher Jain	No
0114	Mayo Clinic - Rochester	Colleen Lane	No
0114	Mayo Clinic - Rochester	Grace Lin	No
0114	Mayo Clinic - Rochester	Kazunori Omote	No
0114	Mayo Clinic - Rochester	Sorin Pislary	No
0114	Mayo Clinic - Rochester	Yogesh Reddy	No
0114	Mayo Clinic - Rochester	Guy Reeder	No
0114	Mayo Clinic - Rochester	Hidemi Sorimachi	No
0115	University of Michigan Health Systems	Scott Hummel	Yes
0115	University of Michigan Health Systems	Stanley Chetcuti	No
0115	University of Michigan Health Systems	Sarah Gualano	No
0115	University of Michigan Health Systems	Matthew Koneruan	No
0115	University of Michigan Health Systems	Victor Moles	No
0115	University of Michigan Health Systems	Scott Visovatti	No
0117	Cardiovascular Institute of the South	Peter Fail	Yes
0117	Cardiovascular Institute of the South	Pradeep Nair	No
0117	Cardiovascular Institute of the South	Vinod Nair	No
0118	Ochsner Clinic	Selim Krim	Yes

Site number	Institution	Investigator	Principal investigator
0118	Ochsner Clinic	Stephen Jenkins	No
0118	Ochsner Clinic	Hamang Patel	No
0119	Yale New Haven Hospital	Joseph Akar	Yes
0119	Yale New Haven Hospital	Lavanya Bellumkonda	No
0119	Yale New Haven Hospital	James Freeman	No
0119	Yale New Haven Hospital	Daniel Jacoby	No
0120	University of Pennsylvania	Jeremy Mazurek	Yes
0120	University of Pennsylvania	Rhondalyn Forde-McLean	No
0120	University of Pennsylvania	Howard Herrmann	No
0120	University of Pennsylvania	Kenneth Margulies	No
0120	University of Pennsylvania	Joyce Wald	No
0121	St. Luke's Hospital Mid America Heart Institute	Anthony Magalski	Yes
0121	St. Luke's Hospital Mid America Heart Institute	Bethany Austin	No
0121	St. Luke's Hospital Mid America Heart Institute	David Cohen	No
0121	St. Luke's Hospital Mid America Heart Institute	Mark Everley	No
0121	St. Luke's Hospital Mid America Heart Institute	Andrew Kao	No
0121	St. Luke's Hospital Mid America Heart Institute	Taiyeb Khumri	No
0121	St. Luke's Hospital Mid America Heart Institute	Stephanie Lawhorn	No
0121	St. Luke's Hospital Mid America Heart Institute	Michael Nasif	No
0121	St. Luke's Hospital Mid America Heart Institute	John Saxon	No
0121	St. Luke's Hospital Mid America Heart Institute	Brett Sperry	No
0121	St. Luke's Hospital Mid America Heart Institute	Deepthi Vodnala	No
0123	Tufts New England Medical Center	Amanda Vest	Yes
0123	Tufts New England Medical Center	Michael Kiernan	No
0123	Tufts New England Medical Center	Carey Kimmelstiel	No
0125	Kaiser Permanente San Francisco Medical Center	Alicia Romero	Yes
0125	Kaiser Permanente San Francisco Medical Center	Ivy Ku	No
0125	Kaiser Permanente San Francisco Medical Center	Dana McGlothin	No
0125	Kaiser Permanente San Francisco Medical Center	Jacob Mishell	No
0125	Kaiser Permanente San Francisco Medical Center	Andrew Rassi	No
0126	Hackensack University Medical Center	Kumar Satya	Yes
0126	Hackensack University Medical Center	Tilak Pasala	No
0126	Hackensack University Medical Center	Lucy Safi	No
0128	Duke University Medical Center	Kishan Parikh	Yes
0128	Duke University Medical Center	Richard Krasuski	No
0128	Duke University Medical Center	Chetan Patel	No
0130	Christ Hospital	Eugene Chung	Yes

Site number	Institution	Investigator	Principal investigator
0130	Christ Hospital	Joseph Choo	No
0130	Christ Hospital	Gregory Egnaczyk	No
0130	Christ Hospital	Michael Jennings	No
0130	Christ Hospital	Timothy Raymond	No
0130	Christ Hospital	Satya Shreenivas	No
0132	Tallahassee Research Institute, Inc.	Thomas Noel	Yes
0132	Tallahassee Research Institute, Inc.	Gian Carlo Giove	No
0132	Tallahassee Research Institute, Inc.	Gregory Hartlage	No
0134	Intercoastal Medical Group	Hakim Morsli	Yes
0135	Scripps Clinic	Rajeev Mohan	Yes
0135	Scripps Clinic	Dhaval Divaker Desai	No
0135	Scripps Clinic	Thomas Heywood	No
0135	Scripps Clinic	Ravi Parikh	No
0135	Scripps Clinic	Matthew Price	No
0135	Scripps Clinic	Daniel Pu	No
0135	Scripps Clinic	David Rubenson	No
0135	Scripps Clinic	Ajay Srivastava	No
0135	Scripps Clinic	Paul Teirstein	No
0137	University of Virginia	Sula Mazimba	Yes
0137	University of Virginia	Monammad Abuannadi	No
0137	University of Virginia	James Bergin	No
0137	University of Virginia	Andrew Buda	No
0137	University of Virginia	Scott Lim	No
0137	University of Virginia	Andrew Minalek	No
0137	University of Virginia	Michael Ragosta	No
0137	University of Virginia	Nishtha Sodhi	No
0137	University of Virginia	Todd Villines	No
0138	University of Chicago Medical Center	John Blair	Yes
0138	University of Chicago Medical Center	Taishi Hirai	No
0138	University of Chicago Medical Center	Roberto Lang	No
0138	University of Chicago Medical Center	Sandeep Nathan	No
0138	University of Chicago Medical Center	Amit Patel	No
0138	University of Chicago Medical Center	Jonathan Paul	No
0138	University of Chicago Medical Center	Atman Shah	No
0138	University of Chicago Medical Center	Bryan Smith	No
0138	University of Chicago Medical Center	Nir Uriel	No
0139	Swedish Medical Center	Sameer Gafoor	Yes

Site number	Institution	Investigator	Principal investigator
0139	Swedish Medical Center	John Mignone	Yes
0139	Swedish Medical Center	Adam Gilbert	No
0139	Swedish Medical Center	John Petersen II	No
0139	Swedish Medical Center	Maddy Petrescu	No
0139	Swedish Medical Center	Ming Zhang	No
0141	Intermountain Medical Center	James Orford	Yes
0141	Intermountain Medical Center	Kia Afshar	No
0141	Intermountain Medical Center	Rami Alharethi	No
0141	Intermountain Medical Center	James Richard Harkness	No
0141	Intermountain Medical Center	Virginia Hebl	No
0141	Intermountain Medical Center	Georges Kfoury	No
0141	Intermountain Medical Center	Michael McCulloch	No
0141	Intermountain Medical Center	Brian Whisenant	No
0142	Morristown Memorial Hospital	Robert Kipperman	Yes
0142	Morristown Memorial Hospital	Philippe Genereux	No
0143	UPMC Presbyterian Hospital	Gavin Hickey	Yes
0143	UPMC Presbyterian Hospital	William Katz	No
0143	UPMC Presbyterian Hospital	Jennifer Kilner	No
0143	UPMC Presbyterian Hospital	Michael Mathier	No
0143	UPMC Presbyterian Hospital	Michael Risbano	No
0143	UPMC Presbyterian Hospital	Erik Schelbert	No
0143	UPMC Presbyterian Hospital	Marc Simon	No
0143	UPMC Presbyterian Hospital	Conrad Smith	No
0145	University of Texas Health Science Center at San Antonio	Steven Bailey	Yes
0145	University of Texas Health Science Center at San Antonio	Lesley Allen	No
0145	University of Texas Health Science Center at San Antonio	Ahmed Almomani	No
0145	University of Texas Health Science Center at San Antonio	Michael Kwan	No
0145	University of Texas Health Science Center at San Antonio	Anjlee Mehta	No
0145	University of Texas Health Science Center at San Antonio	Jason Phillips	No
0146	Minneapolis Heart Institute Foundation	Michael Samara	Yes
0146	Minneapolis Heart Institute Foundation	Richard Bae	No
0146	Minneapolis Heart Institute Foundation	Mosi Bennett	No
0146	Minneapolis Heart Institute Foundation	Nicholas Burke	No
0146	Minneapolis Heart Institute Foundation	Jay Desmond	No
0146	Minneapolis Heart Institute Foundation	Mario Goessl	No
0146	Minneapolis Heart Institute Foundation	Mario Gossl	No
0146	Minneapolis Heart Institute Foundation	Kevin Harris	No

Site number	Institution	Investigator	Principal investigator
0146	Minneapolis Heart Institute Foundation	David Lin	No
0146	Minneapolis Heart Institute Foundation	Jay Traverse	No
0147	Cleveland Clinic	Randall Starling	Yes
0147	Cleveland Clinic	Sanjeeb Bhattacharya	No
0147	Cleveland Clinic	Emanauel Finet	No
0147	Cleveland Clinic	Samir Kapadia	No
0147	Cleveland Clinic	Amar Krishnaswamy	No
0147	Cleveland Clinic	Wilson Tang	No
0150	Medstar Washington Hospital Center	Cyrus Hadadi	Yes
0150	Medstar Washington Hospital Center	Itsik Ben-Dor	No
0150	Medstar Washington Hospital Center	Sandeep Jani	No
0150	Medstar Washington Hospital Center	Lowell Satler	No
0150	Medstar Washington Hospital Center	Ron Waksman	No
0150	Medstar Washington Hospital Center	Zuyue Wang	No
0150	Medstar Washington Hospital Center	Gaby Weissman	No
0151	Baylor University Medical Center	Cesar Guerrero-Miranda	Yes
0151	Baylor University Medical Center	Alan Andy	No
0151	Baylor University Medical Center	Manish Assar	No
0151	Baylor University Medical Center	Paul Grayburn	No
0151	Baylor University Medical Center	Shelley Hall	No
0151	Baylor University Medical Center	Praveen Rao	No
0151	Baylor University Medical Center	Melody Sherwood	No
0153	Houston Methodist Willowbrook Hospital	Imad Hussain	Yes
0153	Houston Methodist Willowbrook Hospital	Ashrith Guha	No
0153	Houston Methodist Willowbrook Hospital	Chun Lin	No
0153	Houston Methodist Willowbrook Hospital	Faisal Nabi	No
0155	Holy Cross Hospital	Joshua Larned	Yes
0155	Holy Cross Hospital	Vicente Font	No
0155	Holy Cross Hospital	Alexander Llanos	No
0157	Virginia Commonwealth University Medical Center	Zachary Gertz	Yes
0157	Virginia Commonwealth University Medical Center	Andrew Andreae	No
0157	Virginia Commonwealth University Medical Center	Richard Cooke	No
0157	Virginia Commonwealth University Medical Center	Jayanthi Konery	No
0157	Virginia Commonwealth University Medical Center	Barbara Lawson	No
0157	Virginia Commonwealth University Medical Center	Sarah Pacinili	No
0157	Virginia Commonwealth University Medical Center	Krishnashee Rao	No
0157	Virginia Commonwealth University Medical Center	Keyur Shah	No

Site number	Institution	Investigator	Principal investigator
0157	Virginia Commonwealth University Medical Center	Melissa Smallfield	No
0157	Virginia Commonwealth University Medical Center	Inna Tchoukina	No
0159	University of Utah Medical Center	John Ryan	Yes
0159	University of Utah Medical Center	Erin Michaelis	No
0159	University of Utah Medical Center	Anwar Tandar	No
0159	University of Utah Medical Center	Fred Welt	No
0159	University of Utah Medical Center	Brent Wilson	No
0162	South Denver Cardiology Associates, PC	Ira Dauber	Yes
0162	South Denver Cardiology Associates, PC	Lee MacDonald	No
0164	Cleveland Clinic Florida	Emad Hakemi	Yes
0164	Cleveland Clinic Florida	Elsy Navas	No
0164	Cleveland Clinic Florida	Yordanka Reyna	No
0165	Baylor College of Medicine	Ajith Nair	Yes
0165	Baylor College of Medicine	Andrew Civitello	No
0165	Baylor College of Medicine	Guilherme Silva	No
0165	Baylor College of Medicine	Leonardo Simpson	No
0166	Lancaster General Hospital	Amit Varma	Yes
0166	Lancaster General Hospital	Rupal Dumasia	No
0166	Lancaster General Hospital	Rahul Jhaveri	No
0168	Kaiser Permanente Medical Center-SD	Jeffrey Cavendish	Yes
0168	Kaiser Permanente Medical Center-SD	Jason Brown	No
0168	Kaiser Permanente Medical Center-SD	Brian Carlos	No
0168	Kaiser Permanente Medical Center-SD	Todd Forster	No
0168	Kaiser Permanente Medical Center-SD	Kamyar Haghani	No
0168	Kaiser Permanente Medical Center-SD	Bahram Khadivi	No
0168	Kaiser Permanente Medical Center-SD	Jenny Papazian	No
0168	Kaiser Permanente Medical Center-SD	Shivak Sharma	No
0168	Kaiser Permanente Medical Center-SD	Elizabeth Wojtowicz	No
0171	Arizona Arrhythmia Research Center	Vijendra Swarup	Yes
0171	Arizona Arrhythmia Research Center	Pranav Doshi	No
0171	Arizona Arrhythmia Research Center	James Dwyer	No
0171	Arizona Arrhythmia Research Center	Robert Lemery	No
0171	Arizona Arrhythmia Research Center	Hursh Naik	No
0171	Arizona Arrhythmia Research Center	Carlos Orrego	No
0173	Froedtert & the Medical College of Wisconsin	David Marks	Yes
0173	Froedtert & the Medical College of Wisconsin	Nunzio Gagiarello	No
0173	Froedtert & the Medical College of Wisconsin	Nicole Lohr	No

Site number	Institution	Investigator	Principal investigator
0173	Froedtert & the Medical College of Wisconsin	Mitchell Saltaberg	No
0201	CHU NANTES HOPITAL LAENNEC	Jean-Noël Trochu	Yes
0201	CHU NANTES HOPITAL LAENNEC	Caroline Cueff de Monchy	No
0201	CHU NANTES HOPITAL LAENNEC	Nicolas Jacob	No
0201	CHU NANTES HOPITAL LAENNEC	Vincent Letocart	No
0201	CHU NANTES HOPITAL LAENNEC	Thibaut Manigold	No
0201	CHU NANTES HOPITAL LAENNEC	Sabine Pattier Al Habash	No
0201	CHU NANTES HOPITAL LAENNEC	Nicolas Piriou	No
0201	CHU NANTES HOPITAL LAENNEC	David Stevant	No
0202	Hôpital Bichat Paris	Guillaume Jondeau	Yes
0202	Hôpital Bichat Paris	Gregory Ducrocq	No
0203	Hopital La Pitie Salpetriere Paris	Richard Isnard	Yes
0203	Hopital La Pitie Salpetriere Paris	Marc Batonga	No
0203	Hopital La Pitie Salpetriere Paris	Nesrine Bouziri	No
0203	Hopital La Pitie Salpetriere Paris	Paul Guedeney	No
0203	Hôpital La Pitié Salpétrière Paris	Nadjib Hammoudi	No
0203	Hôpital La Pitié Salpétrière Paris	Stephane Hatem	No
0203	Hopital La Pitie Salpetriere Paris	Claude Le Feuvre	No
0203	Hôpital La Pitié Salpétrière Paris	Gilles Montalescot	No
0203	Hôpital La Pitié Salpétrière Paris	Francoise Pousset	No
0203	Hopital La Pitie Salpetriere Paris	Michel Zeitouni	No
0204	CHU Rennes France	Erwan Donal	Yes
0204	CHU Rennes France	Vincent Auffret	No
0204	CHU Rennes France	Celine Chabanne	No
0204	CHU Rennes France	Edouard Collette	No
0204	CHU Rennes France	Maxime Fournet	No
0204	CHU Rennes France	Elena Galli	No
0204	CHU Rennes France	Guillaume Leurent	No
0204	CHU Rennes France	Auremie Loirat	No
0204	CHU Rennes France	Elise Paven	No
0204	CHU Rennes France	Camille Pichard	No
0205	CHU Rouen France	Fabrice Bauer	Yes
0205	CHU Rouen France	Chali Aludaat	No
0205	CHU Rouen France	Najim Bouzham	No
0205	CHU Rouen France	Anne-Sophia Da Silva	No
0205	CHU Rouen France	Eric Durand	No
0205	CHU Rouen France	Helene Eltchaninoff	No

Site number	Institution	Investigator	Principal investigator
0205	CHU Rouen France	Olivier Raitiere	No
0206	CHU de Dijon-Hôpital Bocage Central	Jean-Christophe Eicher	Yes
0206	CHU de Dijon-Hôpital Bocage Central	Mourad Benalia	No
0206	CHU de Dijon-Hôpital Bocage Central	Gabriel Laurent	No
0206	CHU de Dijon-Hôpital Bocage Central	Luc Lorgis	No
0206	CHU de Dijon-Hôpital Bocage Central	Raphael Robert	No
0301	Onze Lieve Vrouw-Ziekenhuis	Martin Penicka	Yes
0301	Onze Lieve Vrouw-Ziekenhuis	Jozef Bartunek	No
0301	Onze Lieve Vrouw-Ziekenhuis	Frederik van Durme	No
0301	Onze Lieve Vrouw-Ziekenhuis	Sofie Verstreken	No
0302	AZ ST JAN Brugge Oostende AV	Jan van der Heyden	Yes
0302	AZ ST JAN Brugge Oostende AV	Philippe Debonnaire	No
0302	AZ ST JAN Brugge Oostende AV	Yves Vandekerckhove	No
0401	University Medical Center Groningen	Erik Lipsic	Yes
0401	University Medical Center Groningen	Yuri Blaauw	No
0401	University Medical Center Groningen	H. E de Groot	No
0401	University Medical Center Groningen	Elke Hoendermis	No
0401	University Medical Center Groningen	Femlee Prins	No
0401	University Medical Center Groningen	Laurens Teeuwen	No
0401	University Medical Center Groningen	Paulien van Dorp	No
0401	University Medical Center Groningen	Jost van Melle	No
0401	University Medical Center Groningen	Hendrick Wilemsen	No
0402	St Antonius Ziekenhuis Nieuwegein	Martijn Post	Yes
0402	St Antonius Ziekenhuis Nieuwegein	Mike Bosschaert	No
0402	St Antonius Ziekenhuis Nieuwegein	Livia Gheorghe	No
0402	St Antonius Ziekenhuis Nieuwegein	Johannes (Hans) Kelder	No
0402	St Antonius Ziekenhuis Nieuwegein	Bernard Rensing	No
0402	St Antonius Ziekenhuis Nieuwegein	MJ Suttorp	No
0402	St Antonius Ziekenhuis Nieuwegein	Bertinel van den Akker	No
0403	VU University Medical Center	Louis Handoko	Yes
0403	VU University Medical Center	Cornelis Allaart	No
0403	VU University Medical Center	Marco Gotte	No
0403	VU University Medical Center	Otto Kamp	No
0403	VU University Medical Center	Michiel Kemme	No
0403	VU University Medical Center	Koenraad Marques	No
0403	VU University Medical Center	Ramon van Loon	No
0403	VU University Medical Center	Cornelius Verouden	No

Site number	Institution	Investigator	Principal investigator
0404	Maastricht Heart+Vascular Center (HVC)	Vanessa van Empel	Yes
0404	Maastricht Heart+Vascular Center (HVC)	Christian knackstedt	No
0404	Maastricht Heart+Vascular Center (HVC)	Sebastian Streukens	No
0404	Maastricht Heart+Vascular Center (HVC)	Jindrich Vainer	No
0404	Maastricht Heart+Vascular Center (HVC)	Jerremy Weerts	No
0501	Golden Jubilee National Hospital	Mark Petrie	Yes
0501	Golden Jubilee National Hospital	Colin Berry	No
0501	Golden Jubilee National Hospital	Ross Campbell	No
0501	Golden Jubilee National Hospital	Roy Gardner	No
0501	Golden Jubilee National Hospital	Johanna Osmanska	No
0501	Golden Jubilee National Hospital	Gareth Padfield	No
0501	Golden Jubilee National Hospital	Benjamin Smith	No
0501	Golden Jubilee National Hospital	Allison Smyth	No
0501	Golden Jubilee National Hospital	Piotr Sonecki	No
0501	Golden Jubilee National Hospital	Nicki Walker	No
0501	Golden Jubilee National Hospital	Gary Wright	No
0503	Guy's and St Thomas' NHS Foundation Trust	Tiffany Patterson	Yes
0503	Guy's and St Thomas' NHS Foundation Trust	Chris Allen	No
0503	Guy's and St Thomas' NHS Foundation Trust	Jospeh Jubin	No
0503	Guy's and St Thomas' NHS Foundation Trust	Bradley Porter	No
0503	Guy's and St Thomas' NHS Foundation Trust	Ronak Rajani	No
0601	The Alfred Hospital	David Kaye	Yes
0601	The Alfred Hospital	Antony Walton	No
0602	St. Vincents Hospital Sydney	Christopher Hayward	Yes
0602	St. Vincents Hospital Sydney	David Muller	No
0603	Prince Charles Hospital	Scott Mckenzie	Yes
0604	John Hunter Hospital	Aaron Sverdlov	Yes
0604	John Hunter Hospital	Andrew Boyle	No
0604	John Hunter Hospital	Nicholas Collins	No
0604	John Hunter Hospital	Stuart Turner	No
0605	Concord Hospital - Australia	Andrew Sindone	Yes
0605	Concord Hospital - Australia	Andy Yong	No
0606	Royal Prince Alfred Hospital	Michele McGrady	Yes
0606	Royal Prince Alfred Hospital	Sanjay Patel	No
0702	Medical University of Graz	Andreas Zirlik	Yes
0702	Medical University of Graz	Heiko Bugger	No
0702	Medical University of Graz	Eva Buschmann	No

Site number	Institution	Investigator	Principal investigator
0702	Medical University of Graz	Friedrich Fruhwald	No
0702	Universitäts-Herzzentrum: Klinik für Kardiologie und Angiologie I	Johannes Gollmer	No
0702	Medical University of Graz	Johannes Gollmer	No
0702	Medical University of Graz	Elle Nierdl	No
0702	Medical University of Graz	Albrecht Schmidt	No
0702	Medical University of Graz	Nicolas Verheyen	No
0801	University Hospital Centre	Maja Cikes	Yes
0801	University Hospital Centre	Josko Bulum	No
0801	University Hospital Centre	Nina Jakus	No
0801	University Hospital Centre	Hrvoje Jurin	No
0801	University Hospital Centre	Davor Micilic	No
0801	University Hospital Centre	Marijan Pasalic	No
0801	University Hospital Centre	Ivo Planinc	No
0801	University Hospital Centre	Ivan Prepolec	No
0801	University Hospital Centre	Bosko Skoric	No
0801	University Hospital Centre	Vedran Velagic	No
0901	Rigshospitalet Copenhagen	Finn Gustafsson	Yes
0901	Rigshospitalet Copenhagen	Kiran Mirza	No
0901	Rigshospitalet Copenhagen	Lars Soendergaard	No
1001	University of Milano	Francesco Bandera	Yes
1001	University of Milano	Roberto Arosio	No
1001	University of Milano	Alessia Spina	No
1101	Fourth Military Hospital Wroclaw	Bartek Krakowiak	Yes
1101	Fourth Military Hospital Wroclaw	Radoslaw Antoniak	No
1101	Fourth Military Hospital Wroclaw	Grzegorz Cielinski	No
1101	Fourth Military Hospital Wroclaw	Eliza Gladysz-Zabrzenska	No
1101	Fourth Military Hospital Wroclaw	Marta Glanoska	No
1101	Fourth Military Hospital Wroclaw	Aneta Kosiorek	No
1101	Fourth Military Hospital Wroclaw	Adrian Lis	No
1101	Fourth Military Hospital Wroclaw	Krysztof Reczuch	No
1101	Fourth Military Hospital Wroclaw	Mateusz Sokolski	No
1101	Fourth Military Hospital Wroclaw	Krystof Toczek	No
1101	Fourth Military Hospital Wroclaw	Tomasz Walczak	No
1101	Fourth Military Hospital Wroclaw	Anna Zapolska	No
1201	Hospital Clinico y Provincial de Barcelona	Xavier Freixa	Yes
1201	Hospital Clinico y Provincial de Barcelona	Miguel Camafort	No
1201	Hospital Clinico y Provincial de Barcelona	Maria Angeles Castel	No

Site number	Institution	Investigator	Principal investigator
1201	Hospital Clinico y Provincial de Barcelona	Marta Farrero	No
1201	Hospital Clinico y Provincial de Barcelona	Ana Garcia	No
1201	Hospital Clinico y Provincial de Barcelona	Laura Sanchis	No
1302	Hamilton Health Sciences, Hamilton, Ontario	Shamir Mehta	Yes
1302	Hamilton Health Sciences, Hamilton, Ontario	Koon Teo	No
1401	Georg-August Universität Gottingen	Gerd Hasenfuss	Yes
1401	Georg-August Universität Gottingen	Soren Jan Backaus	No
1401	Georg-August Universität Gottingen	Bo Eric Beutner	No
1401	Georg-August Universität Gottingen	Mohamed Chebboki	No
1401	Georg-August Universität Gottingen	Kristian HellenKamp	No
1401	Georg-August Universität Gottingen	Claudius Jacobshagen	No
1401	Georg-August Universität Gottingen	Torben Lange	No
1401	Georg-August Universität Gottingen	Tim Seidler	No
1401	Georg-August Universität Gottingen	Karl Toischer	No
1401	Georg-August Universität Gottingen	Frieder Wolf	No
1403	Universitätklinikum Dusseldorf	Ralf Westenfeld	Yes
1403	Universitätklinikum Dusseldorf	Florian Bonner	No
1403	Universitätklinikum Dusseldorf	Gulsum Erkilet	No
1403	Universitätklinikum Dusseldorf	Patrick Horn	No
1403	Universitätklinikum Dusseldorf	Anasthasios Karathanos	No
1403	Universitätklinikum Dusseldorf	Georg Wolff	No
1403	Universitätklinikum Dusseldorf	Tobias Zeus	No
1404	Cardiologicum Hamburg	Martin Bergmann	Yes
1404	Cardiologicum Hamburg	Vagia Limperaki	No
1404	Cardiologicum Hamburg	Christina Paitazoglou	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Tobias Wengenmayer	Yes
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Alexander Asmussen	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Nadine Gauchel	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Maximilian Holscher	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Christoph Oliver	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Alexander Peikert	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Haitham Saideldeen	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Peter Stachon	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Constantin Von Zur Mulhen	No
1405	Universitäts-Herzzentrum: Klinik für Kardiologie	Dennis Wolf	No
1406	Charité Universitätsmedizin	Burkert Pieske	Yes
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Site number	Institution	Investigator	Principal investigator
1406	Charité Universitätsmedizin	Sabine Hassfeld	No
1406	Charité Universitätsmedizin	Frank Heinzel	No
1406	Charité Universitätsmedizin	Felix Hodendanner	No
1406	Charité Universitätsmedizin	Abdul Parwani	No
1406	Charité Universitätsmedizin	Cristina Rozados	No
1406	Charité Universitätsmedizin	Franziska Schussler-Hahn	No
1406	Charité Universitätsmedizin	Tobias-Daniel Trippel	No
1406	Charité Universitätsmedizin	Carsten Tschope	No
1406	Charité Universitätsmedizin	Veronica Zach	No
1407	Kerckhoff Heart and Thoraxcenter	Moritz Hass	Yes
1407	Kerckhoff Heart and Thoraxcenter	Ulrich Fischer-Rasokat	No
1407	Kerckhoff Heart and Thoraxcenter	Moritz Haas	No
1407	Kerckhoff Heart and Thoraxcenter	Christian Hamm	No
1407	Kerckhoff Heart and Thoraxcenter	Christoph Liebetrau	No
1407	Kerckhoff Heart and Thoraxcenter	Dirk Muhlbauer	No
1407	Kerckhoff Heart and Thoraxcenter	Mattias Rademann	No
1407	Kerckhoff Heart and Thoraxcenter	Andreas Rieth	No
1407	Kerckhoff Heart and Thoraxcenter	Maren Weferling	No
1408	BG Klinikum Unfallkrankenhaus	Sebastian Winkler	Yes
1408	BG Klinikum Unfallkrankenhaus	Susan Beckmann	No
1408	BG Klinikum Unfallkrankenhaus	Steffen Bohl	No
1408	BG Klinikum Unfallkrankenhaus	Leonhard Bruch	No
1408	BG Klinikum Unfallkrankenhaus	Katrin Schueler (Winkelhofer)	No
1408	BG Klinikum Unfallkrankenhaus	Mirko Seidel	No
1408	BG Klinikum Unfallkrankenhaus	Vasiliki Trikalinou	No
1408	BG Klinikum Unfallkrankenhaus	Rainer Wasielewski	No
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1409	Heart Center of the University of Leipzig	Ingo Dahnaert	No
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1409	Heart Center of the University of Leipzig	Silke John	No
1409	Heart Center of the University of Leipzig	Karl-Patrik Kresoja	No
1409	Heart Center of the University of Leipzig	Matthias Lerche	No
1409	Heart Center of the University of Leipzig	Phillip Munch	No
1409	Heart Center of the University of Leipzig	Danilo Obradovic	No
1409	Heart Center of the University of Leipzig	Karl-Philip Rommel	No
1409	Heart Center of the University of Leipzig	Markus Sandri	No

Site number	Institution	Investigator	Principal investigator
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1409	Heart Center of the University of Leipzig	Maximilian Von Roeder	No
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1411	University Medical Center Hamburg-Eppendorf (UKE)	Christina Magnussen	No
1411	University Medical Center Hamburg-Eppendorf (UKE)	Susanne Schmitt	No
1411	University Medical Center Hamburg-Eppendorf (UKE)	Niklas Schofer	No
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1413	Klinikum der Universität Munchen	Daniel Braun	No
1413	Klinikum der Universität Munchen	Philip Doldi	No
1413	Klinikum der Universität Munchen	Michael Nabauer	No
1413	Klinikum der Universität Munchen	Mathias Orban	No
1413	Klinikum der Universität Munchen	Thomas Stocker	No
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1414	University of Heidelberg	Jan Beckendorf	No
1414	University of Heidelberg	Nicolas Geis	No
1414	University of Heidelberg	Bruna Gomes	No
1414	University of Heidelberg	Leonie Grossekettler	No
1414	University of Heidelberg	Sonia Hamed	No
1414	University of Heidelberg	Michael Kreusser	No
1414	University of Heidelberg	Phillip Schelgel	No
1414	University of Heidelberg	Philipp Schlegel	No
1414	University of Heidelberg	Martin Volz	No
1503	Toyama University Hospital	Koichiro Kinugawa	Yes
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1503	Toyama University Hospital	Hiroshi Ueno	No
1504	National Cerebral and Cardiovascular Center (Osaka)	Chisato Izumi	Yes
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1508	Tottori University Hospital	Yoshiharu Kinugasa	No
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1508	Tottori University Hospital	Akihiro Okamura	No

Site number	Institution	Investigator	Principal investigator
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Site number	Institution	Study coordinator
0101	Northwestern University	Daniel Roshevsky
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0109	Vanderbilt University Medical Center	Kathy Adams
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0115	University of Michigan Health Systems	Joanna Wells
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0117	Cardiovascular Institute of the South	Darla Patrick
0118	Ochsner Clinic	Monique Pellegrin
0119	Yale New Haven Hospital	Catherine Boyle
0120	University of Pennsylvania	Jessica Cheuvront
0120	University of Pennsylvania	Ryan Manzler
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0123	Tufts New England Medical Center	Didjana Celkupa
0125	Kaiser Permanente San Francisco Medical Center	Isabel Perez
0126	Hackensack University Medical Center	Peter Canino
0128	Duke University Medical Center	Lacey Taylor
0130	Christ Hospital	Linda Pennington
0132	Tallahassee Research Institute, Inc.	Rebecca Plasay
0134	Intercoastal Medical Group	Jeanette Wilson
0135	Scripps Clinic	John Gil-Flamer
0137	University of Virginia	Reanna Panagides
0138	University of Chicago Medical Center	Cynthia Arevalo
0139	Swedish Medical Center	Jennifer Nagel
0141	Intermountain Medical Center	Iris Musso
0142	Morristown Memorial Hospital	Christine Ciprich
0143	UPMC Presbyterian Hospital	RachelMcGargle
0143	UPMC Presbyterian Hospital	Kristin Shoemaker
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0150	Medstar Washington Hospital Center	Etsubdink Aboye

Site number	Institution	Study coordinator
0153	Houston Methodist Willowbrook Hospital	Carol Underwood
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0157	Virginia Commonwealth University Medical Center	Melissa Sears
0159	University of Utah Medical Center	JeffGibbs
0162	South Denver Cardiology Associates, PC	Mary Soltau
0164	Cleveland Clinic Florida	Calvin Killingbeck
0165	Baylor College of Medicine	Gilberto DeFreitas
0166	Lancaster General Hospital	Kay Knepper
0168	Kaiser Permanente Medical Center-SD	Sharon Weaver
0171	Arizona Arrhythmia Research Center	Breanna Pratt
0173	Froedtert & the Medical College of Wisconsin	Mary Wexler
0201	CHU NANTES HOPITAL LAENNEC	Patricia Charpentier
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0203	Hôpital La Pitié Salpétrière Paris	Soraya Merbah
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0205	CHU Rouen France	Nassima Colleville
0206	CHU de Dijon-Hôpital Bocage Central	Frederique Debomy
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0401	University Medical Center Groningen	Trijntje Steenhuis
0402	St Antonius Ziekenhuis Nieuwegein	Joke Helwig
0403	VU University Medical Center	Hanneke Gerritsen
0404	Maastricht Heart+Vascular Center (HVC)	Arlette Peters
0501	Golden Jubilee National Hospital	Val Irvine
0503	Guy's and St Thomas' NHS Foundation Trust	RuthSanchez-Vidal
0601	The Alfred Hospital	Eliza Dean
0602	St. Vincents Hospital Sydney	Clare Coates
0603	Prince Charles Hospital	Estelle Beevors
0604	John Hunter Hospital	Anne Gordon
0605	Concord Hospital - Australia	Yi Hong (Jasmine) Wang
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0801	University Hospital Centre	Filip Puskaric
0801	University Hospital Centre	DorjaSabljak
0901	Rigshospitalet Copenhagen	Rikke Boge Sorensen
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1101	Fourth Military Hospital Wroclaw	Iwona Szemplinska
1102	Wroclaw University Clinical Hospital	Jolanta Drazek
1201	Hospital Clinico y Provincial de Barcelona	Anna Barrabes

Site number	Institution	Study coordinator
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1401	Georg-August Universität Gottingen	Anja Eckermann
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1404	Cardiologicum Hamburg	Kristina Schmidt
1405	Universitäts-Herzzentrum: Klinik für Kardiologie und Angiologie I	Beate Hobmaier
1406	Charité Universitätsmedizin	Jens Brestrich
1407	Kerckhoff Heart and Thoraxcenter	Nicole Engelhardt
1408	BG Klinikum Unfallkrankenhaus	Stefanie Geistert
1409	Heart Center of the University of Leipzig	Josephine Koch
1411	University Medical Center Hamburg-Eppendorf (UKE)	Sonam Sundri
1413	Klinikum der Universität Munchen	Stefanie Menner
1413	Klinikum der Universität Munchen	Diana Rosler
1414	University of Heidelberg	Myriam Wittek

Randomizations by Site

Site Number	Site Name	Location	Date of First Patient Randomized	Date of Last Patient Randomized	Total Number of Patients Randomized
101	Northwestern University	Chicago, IL, US	06JUL2017	09MAR2020	18
102	Evanston Northshore Healthcare	Evanston, IL, US	01FEB2018	30JUL2020	5
104	University of Arizona Medical Center University Campus	Tucson, AZ, US	29NOV2018	17DEC2019	6
105	Massachusetts General Hospital	Boston, MA, US	01MAR2018	25OCT2019	6
108	Medical University of South Carolina	Charleston, SC, US	07SEP2017	23JUL2020	23
109	Vanderbilt University Medical Center	Nashville, TN, US	23APR2018	10FEB2020	5
110	Wake Forest Health Sciences	Winston-Salem, NC, US	22JAN2018	03JUL2019	4
111	Ohio State University Wexner Medical Center	Columbus, OH, US	08JUN2017	23JUL2020	21
113	OhioHealth Research Institute	Mansfield, OH, US	27OCT2017	01MAY2019	3
114	Mayo Clinic - Saint Marys Hospital	Rochester, MN, US	18OCT2017	28JUL2020	24
115	University of Michigan Health Systems	Ann Arbor, MI, US	01FEB2018	20FEB2020	11
117	Cardiovascular Institute of the South	Houma, LA, US	29AUG2017	18FEB2020	16
118	Ochsner Clinic	New Orleans, LA, US	15APR2019	15APR2019	1
119	Yale New Haven Hospital	New Haven, CT, US	09MAR2018	09APR2019	2
120	University of Pennsylvania	Philadelphia, PA, US	27SEP2017	10FEB2020	8
121	St. Luke's Hospital Mid America Heart Institute	Kansas City, MO, US	14MAY2018	10JUL2019	2
123	Tuft's Medical Center	Boston, MA, US	14MAY2018	02OCT2019	2
125	Kaiser Permanente San Francisco Medical Center	San Francisco, CA, US	08FEB2018	28JUL2020	6
126	Hackensack University Medical Center	Hackensack, NJ, US	30MAY2019	17DEC2019	3
128	Duke University	Durham, NC, US	16SEP2019	27JAN2020	4
130	Christ Hospital - Ohio Heart & Vascular Cincinnati	Cincinnati, OH, US	27FEB2018	29JUL2020	15
132	Tallahasse Research Institute	Tallahassee, FL, US	22FEB2018	01FEB2019	4
134	Sarasota Memorial Hospital	Sarasota, FL, US	02NOV2018	12JUN2020	5
135	Scripps Clinic	La Jolla, CA, US	16MAY2018	23JUL2020	23
137	University of Virginia Medical Center	Charlottesville, VA, US	19JUN2018	23JUN2020	6
138	University of Chicago Medical Center	Chicago, IL, US	21SEP2017	01JUL2020	13
139	Swedish Medical Center	Seattle, WA, US	26OCT2018	26OCT2018	1
141	Intermountain Medical Center	Murray, UT, US	05JUL2018	06NOV2018	3
142	Morristown Medical Center	Morristown, NJ, US	23FEB2018	23FEB2018	1
143	UPMC Presbyterian	Pittsburgh,, PA, US	17OCT2017	22JAN2019	2
145	The University of Texas Health Science Center at San Antonio	San Antonio, TX, US	06SEP2018	10JAN2020	4

Site Number	Site Name	Location	Date of First Patient Randomized	Date of Last Patient Randomized	Total Number of Patients Randomized
146	Minneapolis Heart Institute Foundation	Minneapolis, MN, US	07JUN2018	04AUG2020	2
147	Cleveland Clinic Foundation	Cleveland, Ohio, US	24MAY2018	09JAN2020	6
150	MedStar Washington Hospital Center	Washington, DC, US	01MAY2019	01MAY2019	1
151	Baylor University Medical Center	Dallas, TX, US	31MAY2018	22JAN2020	3
153	Houston Methodist	Houston, TX, US	25SEP2018	16JUL2020	4
155	Holy Cross Hospital	Fort Lauderdale, FL, US	18APR2019	30JAN2020	2
157	Virginia Commonwealth University Medical Center	Richmond, VA, US	22MAR2018	23JUL2020	4
159	University of Utah Medical Center	Salt Lake City, UT, US	10JUL2018	02JAN2020	4
162	South Denver Cardiology Associates, PC	Littleton, CO, US	18JUL2018	02OCT2019	11
164	Cleveland Clinic Florida	Weston, FL, US	06DEC2018	20DEC2019	2
165	Baylor College of Medicine	Houston, TX, US	06FEB2019	30JUL2020	7
166	Lancaster General Hospital	Lancaster, PA, US	25JUL2019	25JUL2019	1
168	Kaiser Permanente Medical Center-SD	San Diego, CA, US	27AUG2019	27AUG2019	1
171	Arizona Arrhythmia Research Center	Phoenix, AZ, US	31JAN2019	18JUN2020	41
173	Froedtert & the Medical College of Wisconsin	Milwaukee, WI, US	09JAN2020	09JAN2020	1
201	CHU de Nantes	Nantes, France	20SEP2018	08NOV2019	4
202	Claude Bernard - Bichat Hospital, Paris	Paris, France	10MAY2019	10JUL2020	3
203	Pitié Salpêtrière Hospital, Paris LPS	Paris, France	12JUN2019	15JUL2020	4
204	CHU Rennes France	, France	17JUN2019	05MAR2020	4
205	CHU Rouen France	, France	26SEP2019	26SEP2019	1
206	CHU de Dijon-Hôpital Bocage Central	Dijon, France	28FEB2019	08JUL2020	13
301	Onze Lieve Vrouw-Ziekenhuis, Aalst	Aalst, Belgium	17JAN2018	18SEP2019	5
302	AZ ST JAN Brugge Oostende AV	Brugge, Belgium	28MAR2019	14FEB2020	16
401	University Medical Center Groningen	Groningen, Netherlands	15MAR2018	26SEP2019	7
402	St Antonius Ziekenhuis Nieuwegein	Nieuwegein, Netherlands	31MAY2018	21JAN2020	13
403	VU Medical Center, Amsterdam	Amsterdam, Netherlands	27AUG2019	27AUG2019	1
404	Maastricht Heart+Vascular Center (HVC), Maastricht	Maastricht, Netherlands	13MAR2020	24JUL2020	2
501	Golden Jubilee National Hospital, Glasgow	Glasgow, United Kingdom	26OCT2018	27AUG2019	4
503	Guy's & St Thomas' Hosp. NHS Fnd Trust, London GST	London, United Kingdom	14AUG2018	14AUG2018	2
601	The Alfred Hospital	Prahran, Australia	27FEB2018	17MAR2020	14
602	St. Vincents Hospital Sydney	Darlinghurst, Australia	13NOV2017	17MAR2020	8
603	The Prince Charles Hospital Brisbane	Chermside, Australia	17OCT2017	28JUL2020	9
604	John Hunter Hospital	New Lambton Heights, Australia	09MAR2018	05AUG2020	19

Site Number	Site Name	Location	Date of First Patient Randomized	Date of Last Patient Randomized	Total Number of Patients Randomized
605	Concord Hospital - Australia	Concord, Australia	28JUN2018	07MAR2019	2
606	Royal Prince Alfred Hospital	Camperdown, Australia	13DEC2018	14NOV2019	6
702	Medical University of Graz	Graz, Styria, Austria	18JUL2019	09JUL2020	9
801	Rebro University Hospital Center Zagreb	Zagreb, Croatia	30AUG2018	23JUL2020	5
901	Rigshospitalet Copenhagen	Copenhagen, Denmark	25OCT2018	21FEB2020	4
1001	University of Milano - Italy	San Donato Milanese, Italy	01AUG2018	01AUG2018	1
1101	Fourth Military Hospital Wroclaw - Poland	Wroclaw, Poland	24JUL2018	14NOV2019	4
1201	University Barcelona	Barcelona, Spain	09OCT2019	05FEB2020	2
1302	Hamilton Health Sciences	Hamilton, Canada	26SEP2018	13MAR2020	7
1401	Georg-August Universität Gottingen	Gottingen, Germany	24APR2018	14JUL2020	27
1403	Universitätklinikum Dusseldorf	Düsseldorf, Germany	22AUG2018	10JUL2020	9
1404	Cardiologicum Hamburg	Hamburg, Germany	12JUL2018	14MAY2020	10
1405	Universitäts Herzzentrum Freiburg	Freiburg, Germany	11APR2018	17OCT2019	5
1406	Charité Universitätsmedizin Berlin	Berlin, Germany	23JAN2019	03MAR2020	2
1407	Kerckhoff Heart and Thoraxcenter Bad Nauheim	Bad Nauheim, Germany	20FEB2019	24JUN2020	11
1408	BG Klinikum Unfallkrankenhaus Berlin gGmbH	Berlin, Germany	22MAR2019	15JUL2020	30
1409	Heart Center of the University of Leipzig	Leipzig, Germany	10OCT2018	17JUL2020	16
1411	University Medical Center Hamburg-Eppendorf (UKE)	Hamburg, Germany	19DEC2019	19DEC2019	1
1413	Klinikum der Universität Munchen, Munich	München, Germany	16DEC2019	16DEC2019	1
1414	University of Heidelberg, Heidelberg	Heidelberg, Germany	14FEB2019	14FEB2019	1
1503	Toyama University Hospital	Toyama, Japan	05DEC2019	05DEC2019	1
1504	National Cerebral and Cardiovascular Center (Osaka)	Suita, Japan	21JAN2020	21JAN2020	1
1507	The Hospital of Hyogo College of Medicine	Nishinomiya, Japan	18DEC2019	19FEB2020	2
1508	Tottori University Hospital	Yonago, Japan	18FEB2020	10MAR2020	2
1509	Kyushu University Hospital	Fukuoka, Japan	20JAN2020	20JAN2020	1
Total			**08JUN2017**	**05AUG2020**	**626**

Study Organizations and Committee Members

Principal Investigators

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Donald E. Cutlip, MD

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University of Pennsylvania (Frank Silvestry, MD)

Invasive Hemodynamics Core Laboratory

Cardiovascular Clinical Sciences (Ethan Rowin, MD)

Data Monitoring, Management, and Statistical Analysis Centre

Baim Institute for Clinical Research (Donald Cutlip, MD)

SUPPLEMENTARY METHODS

Inclusion and Exclusion Criteria

Inclusion Criteria
1. Chronic symptomatic HF documented by the following: a. Symptoms of HF requiring current treatment with diuretics for ≥ 30 days **AND** b. NYHA class II if a prior history of > NYHA class II; ***OR*** NYHA class III, or ambulatory NYHA class IV symptoms (paroxysmal nocturnal dyspnea, orthopnea, dyspnea on mild or moderate exertion) at screening visit; or signs (any rales post cough, chest x-ray demonstrating pulmonary congestion,) within past 12 months; **AND** c. ≥ 1 HF hospital admission (with HF as the primary, or secondary diagnosis); or treatment with IV; or the need for intensification of oral diuresis for HF in a healthcare facility within the 12 months prior to study entry; ***OR*** an NT-pro BNP value > 150 pg./ml in normal sinus rhythm, > 450 pg./ml in atrial fibrillation, or a BNP value > 50 pg./ml in normal sinus rhythm, > 150 pg./ml in atrial fibrillation within the past 6 months.
2. Ongoing stable GDMT HF management and management of potential comorbidities according to the 2017 ACC/AHA Guidelines for the Management of HF, with no significant changes (>100% increase or 50% decrease), excluding diuretic dose changes, for a minimum of 4 weeks prior to enrollment which is expected to be maintained for 6 months. Stable management includes a minimum period of 4 weeks post hospitalization for any cause, including treatment with IV diuretics.
3. Age ≥ 40 years old
4. Site determined echocardiographic LV ejection fraction ≥40% within the past 6 months, without documented ejection fraction <30% in the 5 years prior to study entry.
Site determined elevated PCWP with a gradient compared to RAP documented by: a. End-expiratory PCWP during supine ergometer exercise ≥ 25mm Hg, and greater than RAP by ≥ 5 mm Hg.

6. Site determined echocardiographic evidence of diastolic dysfunction documented by one or more of the following: a. LA diameter > 4 cm; or b. Diastolic LA volume > 50, LA volume index > 28 ml/m2 or c. Lateral e' < 10 cm/s; or d. Septal e' < 8 cm/s; or e. Lateral E/e' > 10; or f. Septal E/e' > 15
7. Patient has been informed of the nature of the study, agrees to its provisions and has provided written informed consent, approved by the IRB or EC
8. Patient is willing to comply with clinical investigation procedures and agrees to return for all required follow-up visits, tests, and exams
9. Trans-septal catheterization and femoral vein access is determined to be feasible by site interventional cardiology investigator.
Exclusion Criteria
1. MI and/or percutaneous cardiac intervention within past 3 months; CABG in past 3 months, or current indication for coronary revascularization; AVR (surgical AVR or TAVR) within the past 12 months; or a planned cardiac interventions in the 3 months following enrollment.
2. Cardiac resynchronization therapy initiated within the past 6 months.
3. Advanced heart failure defined as one or more of the below: a. ACC/AHA/ESC Stage D heart failure, Non-ambulatory NYHA Class IV HF; b. Cardiac Index < 2.0 L/min/m^2 c. Inotropic infusion (continuous or intermittent) for EF < 40% within the past 6 months d. Patient is on the cardiac transplant waiting list.
4. Inability to perform 6 minute walk test (distance < 50 m), OR 6 minute walk test > 600 m

5. The patient has verified that the ability to walk 6 minutes is limited primarily by joint, foot, leg, hip or back pain; unsteadiness or dizziness or lifestyle (and not by shortness of breath and/or fatigue and/or chest pain).
6. Unwilling or unable (per PhysIQ protocol) to wear telemonitoring patch.
7. Known clinically significant un-revascularized coronary artery disease, defined as: epicardial coronary artery stenosis with angina or other evidence of ongoing active coronary ischemia.
8. History of stroke, TIA, DVT, or pulmonary emboli within the past 6 months.
9. Known clinically significant untreated carotid artery stenosis likely to require intervention.
10. Presence of hemodynamically significant valve disease assessed by the site cardiologist and defined as: a. Mitral valve disease defined as grade ≥ 3+ MR or > mild MS; OR b. Tricuspid valve regurgitation defined as grade ≥ 2+ TR; OR c. Aortic valve disease defined as ≥ 2+ AR or > moderate AS.
11. Hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis, cardiac amyloidosis or other infiltrative cardiomyopathy (e.g. hemochromatosis, sarcoidosis)
12. Patient is contraindicated to receive either dual antiplatelet therapy, or an oral anticoagulant; or has a documented coagulopathy
13. Atrial fibrillation with resting HR > 100 BPM
14. Resting arterial oxygen saturation < 95% on room air
15. Significant hepatic impairment defined as 3X upper limit of normal of transaminases, total bilirubin, or alkaline phosphatase
16. Right ventricular dysfunction, assessed by the site cardiologist and defined as a. More than mild RV dysfunction as estimated by TTE; OR b. TAPSE < 1.4 cm; OR c. RV size ≥ LV size as estimated by TTE; OR

d. Ultrasound or clinical evidence of congestive hepatopathy; OR e. Evidence of RV dysfunction defined by TTE as an RV fractional area change < 35%;
17. Resting RAP > 14 mmHg
18. Evidence of significant pulmonary hypertension defined as PVR > 3.5 Woods units at rest or at peak exercise
19. Chronic pulmonary disease requiring continuous home oxygen, OR significant chronic pulmonary disease defined as FEV1 < 1L
20. Hemoglobin <10 g/dl
21. Currently participating in an investigational drug or device study that would interfere with the conduct or results of this study. Note: trials requiring extended follow-up for products that were investigational but have since become commercially available are not considered investigational
22. Life expectancy less than 12 months for known non-cardiovascular reasons
23. Echocardiographic evidence of intra-cardiac mass, thrombus or vegetation
24. Known or suspected allergy to nickel
25. Women of child bearing potential
26. Currently requiring dialysis; or estimated-GFR <25ml/min/1.73 m^2 by CKD-Epi equation
27. Systolic blood pressure >170 mm Hg at screening
28. Patients with existing or surgically closed (with a patch) atrial septal defects. Patients with a PFO, who meet PCWP criteria despite the PFO, are not excluded.
29. Patients on significant immunosuppressive treatment or on systemic steroid treatment (>10 mg prednisone/day).
30. Severe obstructive sleep apnea not treated with CPAP or other measures
31. Severe depression and/or anxiety
32. In the opinion of the investigator, the patient is not an appropriate candidate for the study
33. Body mass index >40 kg/m^2

Statistical Analysis of the Primary Endpoint

The primary endpoint was compared between treatments using the Finkelstein-Schoenfeld (F-S) approach, a non-parametric method that allows for prioritization of more clinically important components when comparing two treatments on a composite endpoint. The null and alternative hypotheses are: H0: T=0 vs H1: T≠0 where T is the true value of the Finkelstein-Schoenfeld (F-S) statistic. The hierarchy in the estimation of the F-S statistic T is cardiovascular (CV) mortality/non-fatal ischemic stroke component, followed by the heart failure (HF) event component, followed by the Kansas City Cardiomyopathy Questionnaire (KCCQ) component. Specifically, the F-S statistic T is estimated from the clinical trial sample as follows: The first patient is compared to every patient, one at a time, and this first patient is assigned a score of 1/0/-1 for *each* comparison if this first patient has a better (did not experience CV death/ischemic stroke and the comparator patient did), same, or worse (experienced CV death/ischemic stroke and the comparator patient did not) outcome, respectively. For every pairwise comparison where the score is 0, the first patient is assigned a score of 1/0/-1 depending on whether he/she has a better (less HF events than the comparator patient), same (same number of HF events as the comparator patient), or worse outcome (more HF events than the comparator patient), respectively. Finally, for every pairwise comparison where the score is still 0, the first patient is assigned a score of 1/0/-1 depending on whether he/she has a better (change in 12-month KCCQ score at least 5 points larger than the comparator), same (change in 12-month KCCQ score within +/-5 points of comparator) or worse (change in 12-month KCCQ 5 at least 5 points lower than the comparator). This algorithm is then repeated for every patient in the study. The F-S T value is the sum of the 1/0/-1 scores across all patients in the atrial shunt device treatment group. A T-score significantly larger than 0 indicates the atrial shunt device group has a more favorable distribution of components than the control group. The null hypothesis was tested at a two-sided 0.05 level of significance.

Differential follow-up was handled as follows. The calculation of the Finkelstein-Schoenfeld test statistic involves combining scores that are created by comparing each patient, one at a time, with every other patient in the trial on the endpoint components. As pre-specified in the formal statistical analysis plan, when two patients being compared had different follow-up time, then the comparison was carried out on the minimum of the two patients' follow-up time. The reason any two patients could have different follow-up times is two-fold: (a) the study was pre-specified to end 12 months after the last patient was randomized; all patients were then to be followed to this point or to 24 months after randomization, whichever came first; thus, patients were scheduled to have variable follow-up times (12-24 months); (b) a patient could prematurely withdraw from the study prior to the end of planned follow-up time, including due to non-cardiovascular death. Of the 626 randomised patients, 23 (3.7%) prematurely withdrew from the study (including due to death) by 12 months of follow-up (it was expected at the study design stage that approximately 7.5% of subjects would prematurely withdraw by 12 months). There were similar numbers of patients who withdrew prematurely from the study by 12 months in each treatment arm (3.8% in the shunt device arm, 3.5% in the sham control arm).

Pre-specified Subgroup Analyses

The following pre-specified subgroups were analyzed for statistical interaction with treatment on the outcome of recurrent heart failure events:

- **Categorical variables:** sex (male vs. female); race (white vs. non-white); New York Heart Association class (II vs. III/IV); type of heart failure (heart failure with preserved ejection fraction vs. heart failure with mildly reduced ejection fraction); and diabetes, atrial fibrillation/flutter, coronary artery disease, and prior hospitalisation for heart failure in the past 12 months (presence vs. absence for each).
- **Continuous variables:** age, body mass index, KCCQ overall summary score, Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk score, 6-minute walk test distance, natriuretic peptide level, loop diuretic equivalent dose, tricuspid annular plane systolic excursion, left ventricular global longitudinal strain, left atrial reservoir strain, right ventricular free wall strain, right atrial strain, left atrial volume, right atrial volume, resting hemodynamic variables (central venous pressure, pulmonary vascular resistance, difference between pulmonary capillary wedge pressure [PCWP] and central venous pressure, pulmonary and artery systolic pressure), legs up PCWP, and 20W exercise hemodynamic variables (difference between PCWP and central venous pressure, pulmonary artery systolic pressure, and PCWP V wave).

SUPPLEMENTARY RESULTS

Major Protocol Deviations

There were 15 participants with major protocol deviations, 7 in the active treatment group and 8 in the sham control group. Each of these patients were randomized prior to determination that they did not meet inclusion/exclusion criteria.

- 8/15 did not meet inclusion criteria related to heart failure (e.g., diuretic use, NYHA class) (inclusion criteria #1).
- 2/15 met exclusion criteria related to recent major cardiac procedure (exclusion criteria #1).
- 2/15 met exclusion criteria related to the 6-minute walk test (1 was not able to perform the baseline 6-minute walk test due to hip pain, and 1 stated that exercise capacity was limited to non-cardiac reasons) (exclusion criteria #4 and #5).
- 1/15 did not meet the invasive hemodynamic inclusion criteria (inclusion criteria #5).
- 1/15 met exclusion criteria related to atrial fibrillation (resting heart rate > 100 bpm) (exclusion criteria #13).
- 1/15 did not meet inclusion criteria related to heart failure and invasive hemodynamics and met exclusion criteria related to 6-minute walk test (exercise capacity limited due to non-cardiac reasons) (inclusion criteria #1 and #5; exclusion criteria #5).

Detailed Description of Major Adverse Cardiac Events

Cardiac deaths

- Atrial shunt device: 2 deaths
    - Death #1: At day 100, adjudicated as due to heart failure.
    - Death #2: At day 248, adjudicated as due to heart failure.
- Sham control: 2 deaths
    - Death #1: At day 251, adjudicated as sudden death.
    - Death #2: At day 252, adjudicated as due to heart failure.

Myocardial infarctions

- Atrial shunt device: 5 myocardial infarctions
    - MI #1: At day 0. Chest pain post procedure in a patient with history of CABG. Troponin elevation. Adjudicated as procedure-related by CEC. Angiogram without culprit lesion.
    - MI #2: At day 17. Patient with history of aortic valve replacement and atrial fibrillation; Presented with recurrent atrial firillation and chest pain. Troponin elevation. Probable Type 2 MI.
    - MI #3: At day 171. Patient with history of permanent atrial fibrillation; Presented after orthopedic procedure with GI bleeding, metabolic encephalopathy, renal dysfunction and tachycardia. Troponin elevation consistent with Type 2 MI.
    - MI #4: At day 182. Patient with prior stents presented with chest pain and troponin elevation. Angiogram showed 99% in-stent restenosis. Successful PCI.
    - MI #5: At day 350. Multiple prior hospitalization for HF. Following discharge for HF event presented with chest pain and rising troponin; Referred for angiography. Further details not available.
- Sham control: 1 myocardial infarction
    - MI #1: At day 188. Several prior hospitalizations for HF. During a hospitalization developed chest pain with rising troponin. Angiogram showed occluded posterior descending artery.

Cardiac tamponade events

- Atrial shunt device: 3 cardiac tamponade events
    - Cardiac tamponade #1: At day 0. 1 hour post procedure developed hypotension. Echo showed tamponade. Pericardiocentesis for removal of 476 cc bloody fluid. Following day during sheath removal the patient became hypotensive and unresponsive; Intubated; CT angiography showed left PCA stroke. Underwent thrombectomy. Did not regain consciousness; transitioned to palliative care and died on day 15. Adjudicated as a vascular death by the CEC.
    - Cardiac tamponade #2: At day 3. Presented on day 3 with syncope and acute kidney injury. Echocardiogram showed pericardial effusion with questionable clot and echocardiographic signs of increased pericardial pressure. Period of hypotension. Treated with colchicine. No pericardiocentesis performed. Discharged on day 8 with follow-up echocardiogram.

- Cardiac tamponade #3: At day 0: Chest pain post procedure. Echocardiogram showed large pericardial effusion. Pericardiocentesis with removal of 300 cc of fluid. Hemodynamics not available; CEC adjudicated as tamponade.

Emergency surgery events

- Atrial shunt device: 1 emergency surgery event
  - Emergency surgery event #1: At day 0 for device embolization.

SUPPLEMENTARY TABLES

Supplemental Table 1. Reasons for Screen Failure

Frequency	Explanation	Criteria number
46	Did not meet inclusion criteria for documentation of heart failure	Inclusion #1
37	Hemodynamically significant valve disease	Exclusion #10
36	Participant not willing to comply with study procedures	Inclusion #8
24	Participant was not an appropriate candidate for the study (per investigator)	Exclusion #32
22	Meets right ventricular dysfunction exclusion criteria	Exclusion #16
16	Not on stable heart failure therapy	Inclusion #2
15	Ejection fraction < 40%	Inclusion #4
12	Hemoglobin < 10 g/dl	Exclusion #20
10	Did not meet criteria for diastolic dysfunction on echocardiography	Inclusion #6
9	Dialysis-dependent or GFR < 25 ml/min/1.73 m^2	Exclusion #26
8	6MWT limited by non-cardiac condition	Exclusion #5
7	Resting arterial oxygen saturation < 95% on room air	Exclusion #14
6	BMI > 45 kg/m^2	Exclusion #33
5	6MWT distance < 50 or > 600 meters	Exclusion #4
4	Femoral vein access or transseptal access not feasible	Inclusion #9
4	Recent MI, PCI, CABG, AVR, or planned cardiac intervention	Exclusion #1
3	Hypertrophic, restrictive, or infiltrative cardiomyopathy, or constrictive pericarditis	Exclusion #11
2	Atrial fibrillation with resting HR > 100 BPM	Exclusion #13
2	Clinically significant chronic pulmonary disease (on home oxygen, FEV1 < 1.0 L)	Exclusion #19
2	History of stroke, TIA, DVT, or PE in last 6 months	Exclusion #8
2	Participant did not sign informed consent	Inclusion #7
2	Severe obstructive sleep apnea not treated with CPAP or other measures	Exclusion #30
2	Significant immunosuppressive medication treatment	Exclusion #29
2	Unable to receive dual anti-platelet therapy or documented coagulopathy	Exclusion #12
1	Clinically significant untreated carotid artery stenosis	Exclusion #9
1	Existing or surgically or percutaneously closed atrial septal defect	Exclusion #28
1	Known or suspected allergy to nickel	Exclusion #24
1	Severe depression or anxiety	Exclusion #31
1	Significant hepatic impairment	Exclusion #15
1	Systolic blood pressure > 170 mmHg at screening	Exclusion #27
1	Unwilling or unable to wear telemonitoring patch	Exclusion #6
1	Woman of child-bearing potential	Exclusion #25

Supplemental Table 2. Additional Baseline Characteristics of the Study Population (Physical Characteristics, Laboratory Data, Echocardiographic Characteristics, and Invasive Hemodynamics)

Patient Characteristics	All Randomized Participants (N=626)
Physical characteristics and laboratory data	
Body mass index, kg/m^2	32.0 (27.7, 37.0)
Height, cm	167.3 (160.0, 174.2)
Weight, kg	89.8 (76.9, 105.0)
Heart rate, beats/min	70.0 (62.0, 78.0)
Systolic blood pressure, mmHg	127.0 (115.0, 140.0)
Diastolic blood pressure, mmHg	72.0 (64.0, 80.0)
Hemoglobin, g/dL	12.9 (11.5, 14.1)
Estimated glomerular filtration rate, ml/min/1.73 m^2	56.5 (42.0, 68.0)
Sodium	140.0 (138.0, 142.0)
Potassium	4.3 (4.0, 4.7)
Echocardiographic characteristics	
Septal wall thickness (cm)	1.0 (0.9, 1.1)
Posterior wall thickness (cm)	0.9 (0.8, 1.0)
LV end-diastolic dimension (cm)	4.8 (4.4, 5.2)
LV end-systolic dimension (cm)	3.5 (3.1, 4.0)
Relative wall thickness	0.4 (0.3, 0.4)
LV mass (g)	162.0 (133.0, 202.0)
LV mass index (g/m^2)	80.8 (65.3, 98.4)
LV end-diastolic volume index (ml)	108.0 (90.0, 135.0)
LV end-systolic volume index (ml)	51.0 (40.0, 66.0)
LV ejection fraction (%)	54.3 (50.0, 57.2)
Stroke volume (ml)	66.0 (55.0, 82.0)
LV global longitudinal strain (%)	17.7 (15.4, 20.2)
Early diastolic transmitral (E) velocity (cm/s)	86.0 (69.0, 108.0)
Late diastolic transmitral (A) velocity (cm/s)	75.0 (55.0, 94.0)
E/A ratio	1.1 (0.8, 1.6)
Septal e' velocity (cm/s)	6.0 (5.0, 7.0)
Lateral e' velocity (cm/s)	8.0 (6.0, 10.0)
Average E/e' ratio	12.5 (9.7, 17.0)
RV dimension (cm)	3.3 (3.0, 3.7)
Tricuspid annular plane systolic excursion (cm)	2.0 (1.8, 2.3)
Estimated RA pressure (mmHg)	3.0 (3.0, 3.0)
LA volume index (ml/m^2)	31.1 (24.4, 39.2)
LA reservoir strain (%)	20.3 (14.2, 26.8)
RA reservoir strain (%)	24.0 (17.9, 31.2)
RV free wall strain (%)	22.4 (17.9, 26.0)
RA volume (ml)	50.0 (37.8, 67.8)
Tricuspid regurgitation velocity (cm/s)	261.0 (236.0, 291.8)
Estimated PA systolic pressure (mmHg)	31.0 (26.0, 39.0)
Tricuspid regurgitation severity (0-4)	1.0 (0.5, 1.0)
Pulmonic regurgitation severity (0-4)	0.5 (0.5, 1.0)
Mitral regurgitation severity (0-4)	1.0 (0.5, 1.0)
Aortic regurgitation severity (0-4)	0.0 (0.0, 0.5)
Resting invasive hemodynamics	
Heart rate (bpm)	70.0 (63.0, 80.0)

Patient Characteristics	All Randomized Participants (N=626)
Systolic blood pressure (mmHg)	143.0 (128.0, 158.0)
Right atrial pressure (mmHg)	9.0 (7.0, 12.0)
PA systolic pressure (mmHg)	40.0 (34.0, 50.0)
PA diastolic pressure (mmHg)	19.5 (15.0, 24.0)
PA mean pressure (mmHg)	26.3 (21.7, 32.3)
PA saturation (%)	68.4 (64.2, 72.8)
Pulmonary capillary wedge pressure (mmHg)	18.0 (14.0, 23.0)
Right atrial pressure/PCWP ratio	0.50 (0.41, 0.63)
RV stroke work index (g·m/m^2/beat)	8.7 (6.4, 11.6)
PA pulsatility index	2.4 (1.7, 3.5)
Cardiac output (L/min)	5.3 (4.5, 6.3)
Cardiac index (L/min/m^2)	2.6 (2.2, 3.0)
Systemic vascular resistance (Wood units)	16.2 (13.1, 20.6)
Pulmonary vascular resistance (Wood units)	1.5 (1.1, 2.1)
Legs up invasive hemodynamics	
Right atrial pressure (mmHg)	11.0 (8.0, 15.0)
PA systolic pressure (mmHg)	47.0 (40.0, 58.0)
PA diastolic pressure (mmHg)	23.0 (19.0, 28.0)
Pulmonary capillary wedge pressure (mmHg)	22.0 (18.0, 27.0)
Peak exercise invasive hemodynamics	
Exercise capacity (Watts)	40.0 (20.0, 60.0)
Heart rate (bpm)	100.0 (86.0, 113.0)
Right atrial pressure (mmHg)	18.0 (14.0, 22.0)
PA systolic pressure (mmHg)	70.0 (60.0, 80.0)
PA diastolic pressure (mmHg)	34.0 (29.0, 40.0)
Pulmonary capillary wedge pressure (mmHg)	34.0 (29.0, 40.0)
Cardiac output (L/min)	7.6 (6.1, 9.5)
Cardiac index (L/min/m^2)	3.7 (3.1, 4.5)
PCWP/cardiac output (mmHg/L/min)	4.6 (3.4, 6.0)
Systemic vascular resistance (Wood units)	11.7 (9.0, 15.6)
Pulmonary vascular resistance (Wood units)	1.3 (0.8, 2.0)

LA = left atrial; LV = left ventricular; PA = pulmonary artery; PCWP = pulmonary capillary wedge pressure; RA = right atrial; RV = right ventricular.

Supplemental Table 3. Comparison of Recurrent Heart Failure Event Rate Between Treatment Groups at 3, 6, and 12 Months of Follow-up

Time point	Incidence Rate Ratio [95% CI]*	P-value
At 3-month	1.57 (0.80, 3.08)	0.19
At 6-month	1.47 (0.84, 2.59)	0.18
At 12-month	1.35 (0.84, 2.19)	0.22
At 24-month	1.10 (0.72, 1.67)	0.67

*Values represent comparison of atrial shunt device arm vs. sham control

Supplemental Table 4. Primary and Secondary Efficacy Endpoints in the Per Protocol Population

		P Value
Finkelstein-Schoenfeld statistic, T/SE	-548/3682	0.88
P (Better in Treatment) [95% CI][1]	0.5 (0.46, 0.54)	
Win Ratio [95% CI]	0.98 (0.8, 1.21)	

Components of the Primary Endpoint/Secondary Endpoints	Treatment (N = 288 Patients)	Control (N = 282 Patients)	P Value
Incidence of Time-to-Cardiovascular Death or Non-Fatal Ischemic Stroke at 12 Month[2]	1.39% (4)	0.71% (2)	0.42
Cardiovascular Death	1.04% (3)	0.71% (2)	0.67
Non-fatal Ischemic Stroke	0.35% (1)	0% (0)	0.32
Total rate (first plus recurrent) per patient year of HF admissions or healthcare facility visits for IV diuresis or visits with intensification of oral diuresis for HF up to24 months[3]	0.27	0.25	0.49
Change in KCCQ from Baseline to 12 Months Overall Summary Score[4]			0.75
Mean ± SD (N)	11.5±21.5 (276)	10.4±21.3 (263)	
Median (Q1, Q3)	10.2 (-1.7, 26.8)	9.4 (-2.3, 23.2)	
Range (Min, Max)	(-49.5, 82.3)	(-56.1, 71.9)	
Change in NYHA Class from Baseline to 12 Months[5]			0.005
Median (Q1, Q3)	-1.0 (-1.0, 0.0)	0.0 (-1.0, 0.0)	

[1]Probability of favorable distribution.
[2]From K-M estimates. Log-rank P-value is presented; non-CV death is treated as a competing risk.
[3]Poisson regression was used to compare HF events rates per patient-year.
[4]The p-value for change in KCCQ score from baseline to 12 months was computed using ANCOVA adjusting for baseline score.
[5]The p-value for change in NYHA from baseline to 12 months was tested using the Wilcoxon Rank Sum test.

Supplemental Table 5. Addition of Heart Failure Medications During the Duration of the Trial

Pharmacotherapy	Study visit	Atrial shunt device	Sham control	P-value
SGLT2-inhibitors	Baseline	5/314 (1.6%)	11/312 (3.5%)	0.13
	12 months	10/314 (3.2%)	17/312 (5.4%)	0.16
	24 months	13/314 (4.1%)	23/312 (7.4%)	0.08
Sacubitril/valsartan	Baseline	5/314 (1.6%)	6/312 (1.9%)	0.75
	12 months	4/314 (1.3%)	8/312 (2.6%)	0.24
	24 months	6/314 (1.9%)	9/312 (2.9%)	0.43

Supplemental Table 6. Blinding Questionnaire Results

Visit	Atrial Shunt Device	Sham Control
	Subject-Based (N=314 Patients)	Subject-Based (N=312 Patients)
During Procedure		
Patient blinding not maintained through unblinding visit per protocol	0.32% (1/314)	0.00% (0/312)
Post-procedure through Discharge		
Patient blinding not maintained through unblinding visit per protocol	0.96% (3/314)	0.00% (0/312)
Research staff blinding not maintained	0.32% (1/314)	0.00% (0/312)
2 Weeks post-procedure telephone contact		
Patient blinding not maintained through unblinding visit per protocol	0.64% (2/314)	0.32% (1/312)
Study staff blinding not maintained through unblinding visit per protocol	0.64% (2/314)	0.00% (0/312)
1 Month follow-up visit		
Patient blinding not maintained through unblinding visit per protocol	0.65% (2/310)	0.32% (1/312)
Study staff blinding not maintained through unblinding visit per protocol	0.65% (2/310)	0.32% (1/312)
3 Months follow-up visit		
Patient blinding not maintained through unblinding visit per protocol	0.33% (1/305)	0.00% (0/309)
Study staff blinding not maintained through unblinding visit per protocol	0.33% (1/305)	0.32% (1/309)
6 Months follow-up visit		
Patient blinding not maintained through unblinding visit per protocol	1.31% (4/305)	0.00% (0/306)
Study staff blinding not maintained through unblinding visit per protocol	0.33% (1/305)	0.65% (2/306)
12 Months follow-up visit		
Patient blinding not maintained through unblinding visit per protocol	2.31% (7/303)	0.00% (0/305)
Study staff blinding not maintained through unblinding visit per protocol	0.99% (3/303)	0.33% (1/305)
Total number of patients unblinded by Month 12	**6.69% (21/314)**	**2.24% (7/312)**
Total number of patients in whom blinded study staff became unblinded by Month 12	**3.18% (10/314)**	**1.60% (5/312)**

Supplemental Table 7. Effect of COVID-19 on the Primary Outcome

Primary endpoint	Overall outcome			Pre-COVID-19 outcome		
	Win ratio (95% CI)		P-value	Win ratio (95% CI)		P-value
Composite endpoint	0.98 (0.80, 1.20)		0.85	1.05 (0.74, 1.50)		0.78
Components of the primary endpoint	**Atrial shunt device (N=309)**	**Sham control (N=312)**	**P-value**	**Atrial shunt device (N=95)**	**Sham control (N=101)**	**P-value**
Cardiovascular death or non-fatal ischemic stroke	1.30% (4)	0.65% (2)	0.41	2.12% (2)	2.02% (2)	0.95
CV death	0.98% (3)	0.65% (2)	0.65	2.12% (2)	2..02% (2)	0.95
Non-fatal ischemic stroke	0.33% (1)	0% (0)	0.32	0% (0)	0% (0)	—
Rate of HF hospitalization for IV diuresis or intensification of oral diuresis (per patient-year)	0.28	0.25	0.45	0.36	0.38	0.82
Change in KCCQ overall summary score (mean±SD [N])	11.5±21.5 (282)	10.5±21.2 (269)	0.73	13.2±23.1 (85)	13.0±22.9 (84)	0.75

Supplemental Table 8. Major Vascular and Bleeding Complications

Major vascular or bleeding complications	Atrial shunt device (N=309)		Sham control (N=312)		P-value
	Number of events	% (#) of patients	Number of events	% (#) of patients	
Total[1]	18	4.21% (13)	0	0% (0)	<0.001
Access site hematoma > 5 cm[2]	8	2.59% (8)	0	0% (0)	0.004
Pseudoaneurysm[3]	2	0.65% (2)	0	0% (0)	0.25
AV fistula	0	0% (0)	0	0% (0)	—
Retroperitoneal bleed[4]	2	0.65% (2)	0	0% (0)	0.25
Peripheral ischemia/nerve injury[5]	1	0.32% (1)	0	0% (0)	0.50
Procedure-related transfusion > 1 unit of packed red blood cells[6]	3	0.97% (3)	0	0% (0)	0.12
Vascular surgery repair[7]	2	0.65% (2)	0	0% (0)	0.25

[1]All major vascular or bleeding complications occurred prior to 30 days post-procedure. Of the 13 patients in the treatment group with complications, 8 (61%) had access site hematomas. Overall, 18 events were reported for 14 patients in the treatment arm, with 3 events recorded multiple categories, and 2 events requiring surgical repair (described in detail below).
[2]Eight hematomas: Five (5) direct groin access hematomas w/o transfusion: one required 1 or more units of blood transfusion. Two (2) were due to internal jugular injury for right heart catheterization: one hematoma also resulted in nerve injury and required surgery, and one was in setting of diffuse soft tissue bleeding and probably related to OACs and APT.
[3]Two pseudoaneurysms: one was the complicated case above for RP bleed; one was an incidental finding on CT for GI complaints and was treated with US guided compression.
[4]Two retroperitoneal (RP) bleeds: one was a patient transferred from cath lab to ED and then to a different institution for treatment (eventual surgical diagnosis was ruptured pseudoaneurysm), RP bleed requiring surgery and transfusion; and one was due to (presumed spontaneous) right renal hemorrhage at day 8.
[5]One nerve injury: associated with right internal jugular vein hematoma.
[6]Three procedural transfusions: two were due to blood loss during sheath pulls and drop in hemoglobin, and one was due to retroperitoneal bleed. ;
[7]Two vascular surgery repairs: one was associated with right internal jugular hematoma and nerve injury; one was for ruptured pseudoaneurysm and retroperitoneal bleed.

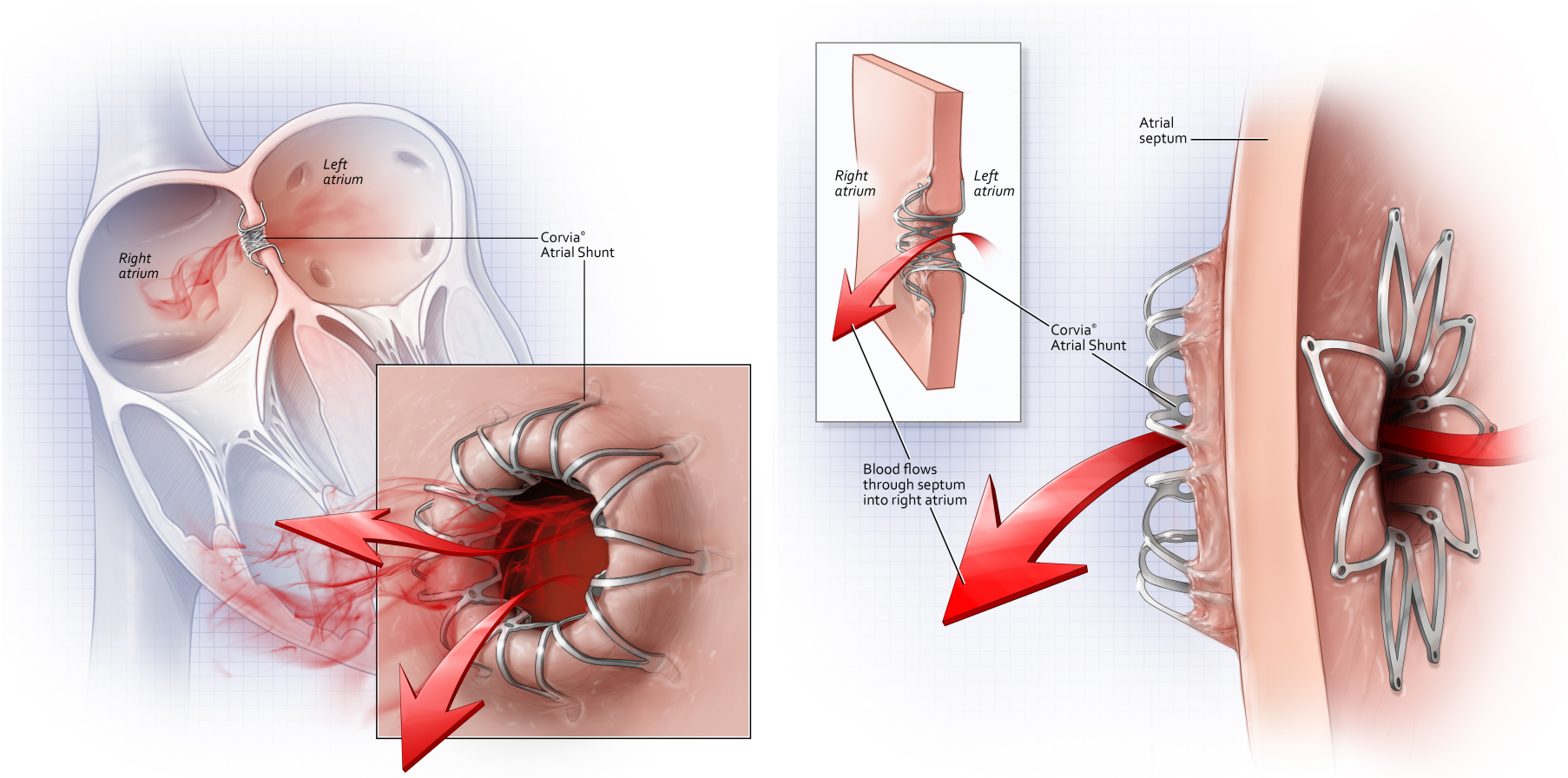
Supplemental Table 9. Kansas City Cardiomyopathy Questionnaire Overall Summary Score: Results from Recent Heart Failure Randomized Clinical Trials

Randomized clinical trial	Ejection fraction cut-off	Total sample size (n)	Follow-up time (weeks)	Mean baseline KCCQ overall summary score	Mean change in KCCQ overall summary score in the control group
REDUCE LAP-HF II	≥40%	**626**	**52**	**45.8**	**+10.3**
PARALLAX*	≥40%	2566	24	52.4	+11.7
TOPCAT-Americas	≥45%	1767	52	57.7	+5.7
DAPA-HF	<40%	4744	32	68.0	+4.5
EMPEROR-Preserved	>40%	5988	52	68.9	+3.0
PANACHE	≥45%	305	20	69.6	+0.9
EMPEROR-Reduced	<40%	3730	52	70.7	+4.7
PARAGON*	≥45%	4822	32	71.4	-2.6
PARADIGM*	<40%	8442	32	72.7	-0.1

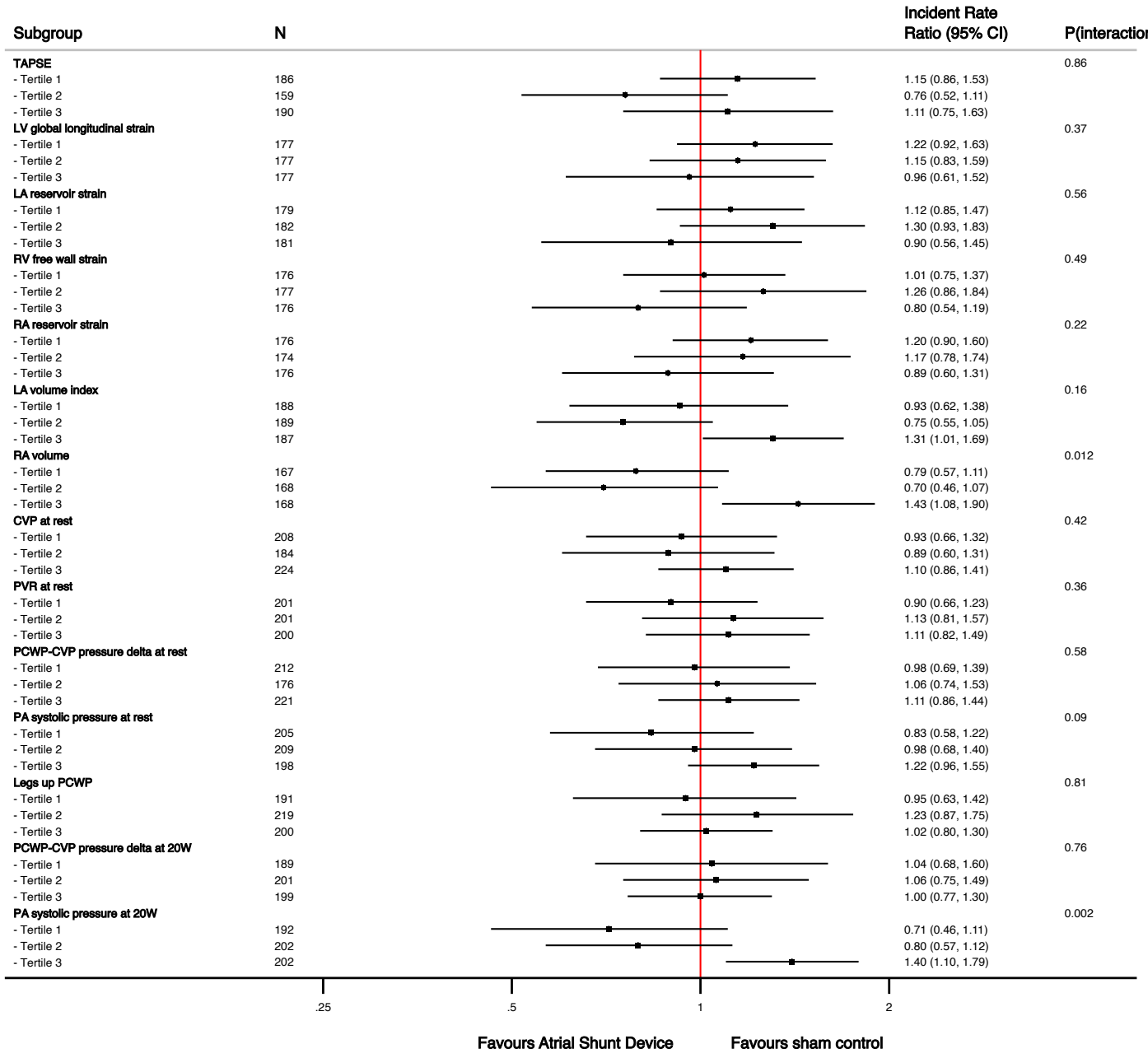
*Control group for PARAGON, PARALLAX, and PARADIGM was valsartan, individualized RAAS therapy (based on baseline ACE-I/ARB use), and enalapril, respectively. Control group was placebo for all other trials.

SUPPLEMENTARY FIGURES

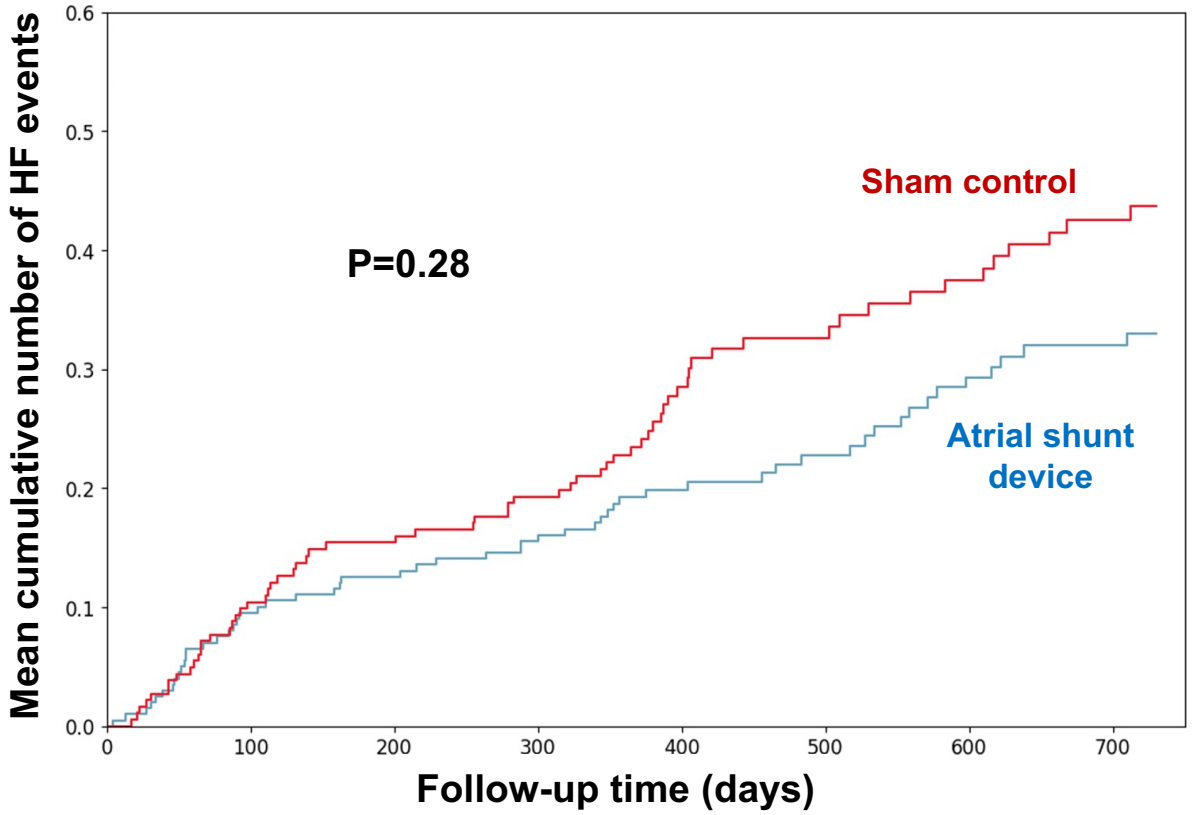
Supplemental Figure 1. Corvia Atrial Shunt Device



Supplemental Figure 2. Forest Plot of Treatment Effect on Recurrent Heart Failure Events by Pre-Specified Subgroups (Echocardiographic and Invasive Hemodynamic Variables)

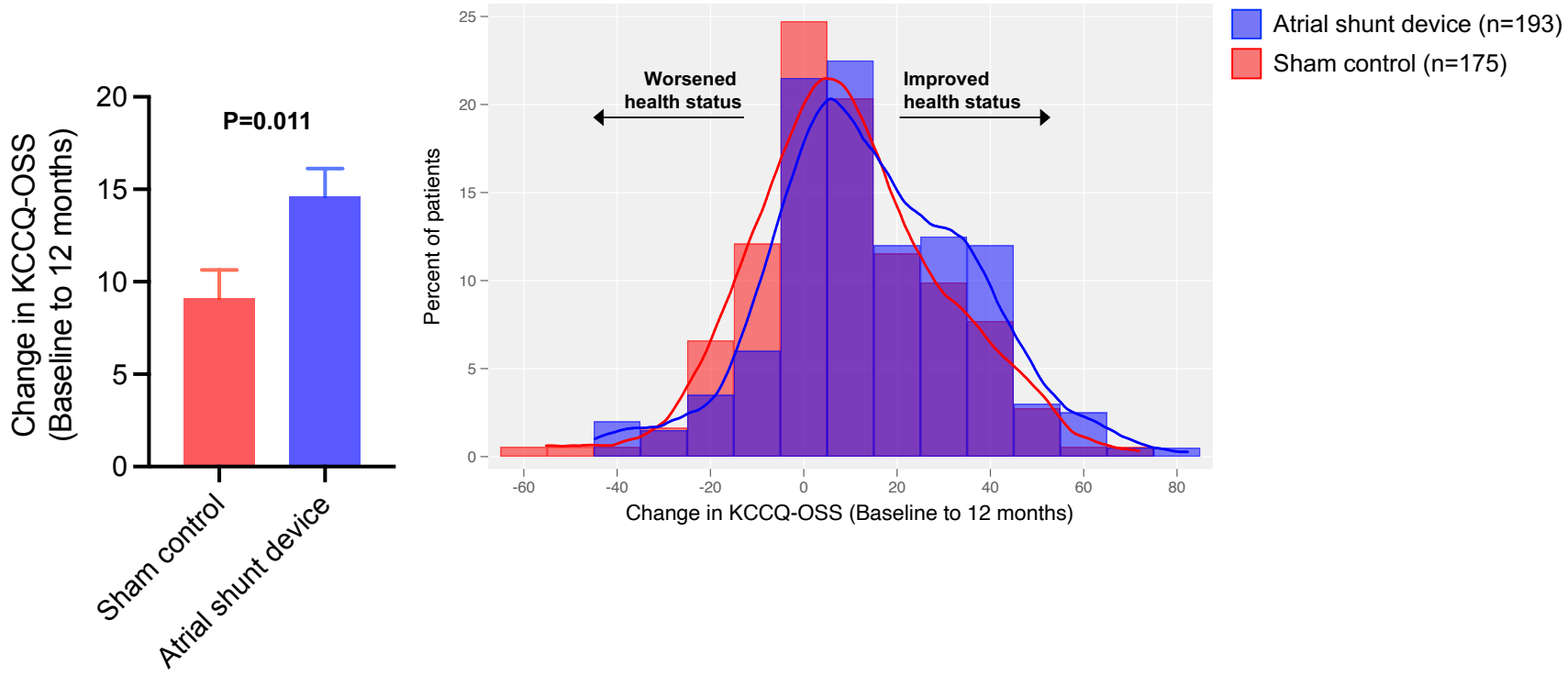


Supplemental Figure 3. Mean Cumulative Heart Failure Events in the Subgroup of Patients with Peak Exercise Pulmonary Vascular Resistance < 1.74 Wood units: Atrial Shunt Device vs. Sham Control



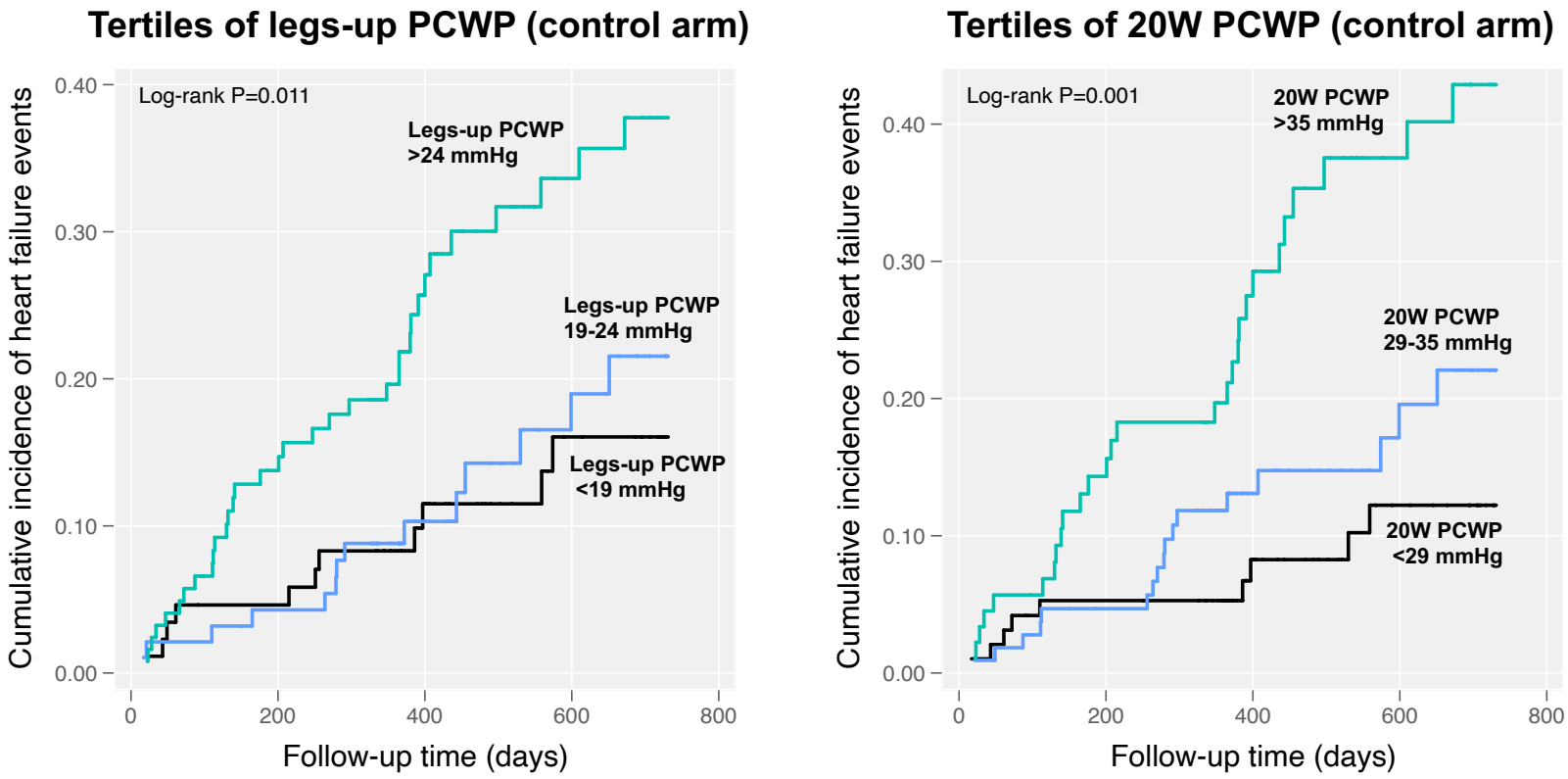
TREATMENT	At risk	200	199	199	199	150	127	117	104
CONTROL	At risk	182	182	180	180	128	105	100	90

Supplemental Figure 4. Change in KCCQ Overall Summary Score from Baseline to 12 Months in the Subgroup of Patients with Peak Exercise Pulmonary Vascular Resistance < 1.74 Wood units: Atrial Shunt Device vs. Sham Control



There were 11% more patients in the atrial shunt device arm who had a marked (≥ 20 point) improvement in KCCQ score at 12 months, and there were 13% fewer patients in the atrial shunt device arm who had a clinically significant worsening (≥ 5 point) reduction in KCCQ score at 12 months, compared to sham control.

Supplemental Figure 5. Association of Tertiles of Legs-up and 20W Exercise Pulmonary Capillary Wedge Pressure with Incident Heart Failure Events in the REDUCE LAP-HF II Trial: Kaplan-Meier Cumulative Incidence Curves



In the REDUCE LAP-HF I trial, legs up PCWP was reduced by a mean of 5.0 mmHg in the shunt-device arm, and 20W PCWP was reduced by a mean of 3.2 mmHg in the shunt device arm. Application of these numbers to the control arm of the REDUCE LAP-HF II trial shows the following:

- Legs-up PCWP and incident HF: HR 0.76 (95% CI 0.64-0.89), p=0.001 for each 5.0 mmHg lowering of legs-up PCWP. Thus, a 5.0 mmHg lower legs-up PCWP is associated with a 24% lower risk of incident HF.
- 20W PCWP and incident HF: HR 0.87 (95% CI 0.80-0.94), p=0.001 for each 3.0 mmHg lowering of 20W PCWP. Thus, a 3.0 mmHg lower 20W PCWP is associated with a 13% lower risk of incident HF.

Supplemental Figure 6. Inverse Association of Baseline Kansas City Cardiomyopathy Questionnaire Overall Summary Score with Improvement in the Control Group in Recent Heart Failure Trials