

## Supplementary Online Content

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### **Complete listing of committees and coordinating centers in the SHINE Trial**

#### **SHINE participating sites that enrolled 0 patients**

#### **List of nonauthor contributors**

**eTable 1.** Additional baseline and treatment information of the patients

**eTable 2.** Secondary analyses of primary and secondary outcomes

**eTable 3.** Baseline characteristics and treatment information by highest enrolling sites vs all other sites by treatment group

**eFigure 1.** Primary efficacy outcome, according to subgroups

**eFigure 2.** Relative risk and 95% confidence intervals for reported serious adverse events

This supplementary material has been provided by the authors to give readers additional information about their work.

## **SHINE Trial: Committees and Coordinating Centers**

In addition to the authors, the following individuals contributed to the SHINE Trial:

### **Executive Committee**

Karen C. Johnston, MD, MSc, William G. Barsan, MD, Valerie L. Durkalski-Mauldin, PhD, Qi Pauls, MS, Kavita Patel, BS, RN, Askiel Bruno, MD, MSc, Kevin M. Barrett, MD, MSc, Christiana E. Hall, MD, MS, Katrina Van de Bruinhorst, MS, Heather M. Haughey, PhD, Sonya A. Gunter, MS, Ruth R.R. Lewis, MS, RN, William Meurer, MD, MS, Valerie Stevenson, BAS, RRT, CCRP, Scott Janis, PhD

### **Recruitment Committee**

Karen C. Johnston, MD, MSc, Askiel Bruno, MD, MSc, Kevin M. Barrett, MD, MSc, Christiana E. Hall, MD, MS, Katrina Van de Bruinhorst, MS, Heather M. Haughey, PhD, Kavita Patel, BS, RN, Ruth R.R. Lewis, MS, RN, Sonya A. Gunter, MS, Amy Fansler, MPH

### **Publication Committee**

Askiel Bruno, MD, MSc, William Meurer, MD, MS, Karen C. Johnston, MD, MSc, Christiana E. Hall, MD, MS, Valerie L. Durkalski-Mauldin, PhD, Robert Silbergleit, MD, Scott Janis, PhD, Amy Fansler, MS

### **NETT Clinical Coordinating Center**

William Barsan, MD, Joy Black, BSN, RN, MS, Allison Kade Fox, MD, MS, Shirley Frederiksen, BSN, MS, Donna Harsh, MS, Ruth R. R. Lewis, MS, RN, William J. Meurer, MD, MS, Arthi Ramakrishnan, MS, CCRP, Robert Silbergleit, MD, Cemal Sozener, MD, MEng, Valerie Stevenson BAS, RRT, CCRP, Carol Van Huysen, BS, CCRP

### **NETT Statistical and Data Coordinating Center**

Valerie L. Durkalski-Mauldin, PhD, Qi Pauls, MS, Kavita Patel, BS, RN, Catherine R. Dillon, MS, Yuko Palesch, PhD, Keith Pauls, BS, Jaemyung Kim, MS, Wenle Zhao, PhD

### **Data and Safety Monitoring Board**

Michael D. Hill, MD, Susan Shapiro Braithwaite, MD, William R. Clarke, PhD, Jennifer Frontera, MD, Kama Guluma, MD, Rema Raman, PhD, Jeffery L. Saver, MD, Joshua N. Goldstein, MD, PhD, Janice Cordell BSN, MPH

### **SHINE Mimic Adjudication Team**

Andrew M. Southerland, MD, MSc, Jeffery A. Switzer, MD

### **Independent Safety Monitor**

Thomas Bleck, MD

### **SHINE Diabetologists**

Mercedes Falciglia, MD

Rattan Juneja, MD

### **Medical Decisions Network, LLC**

Greg Menke, Will Menke, Denise Zito, Charlie Rogers, Sei Kim, Paula Maurer, RN, BSN

**National Institute of Neurological Disorders and Stroke - National Institutes of Health**

Scott Janis, PhD, Carolina Mendoza-Puccini, MD, Janice Cordell BSN, MPH

**SHINE participating sites that enrolled 0 patients**

Hub	Site	Principal Investigator	Primary Study Coordinator
Minnesota	University of Kansas Hospital, Kansas City, KS	Michael Abraham	Alison Boyotston
Ohio State	Miami Valley Hospital, Dayton, OH	John Terry	Angela Shoen
Temple	Hackensack University Medical Center, Hackensack, NJ	Chinwe Ogedegbe	Arelis Villot-Santiago
UCSF	California Pacific Medical Center Davies Campus, San Francisco, CA	Nobl Barazangi	Katie Ponting
UCSF	California Pacific Medical Center Pacific Campus, San Francisco, CA	Nobl Barazangi	Katie Ponting
VCU	VCU Medical Center, Richmond, VA	Warren Felton III	Margot Lee
Wayne	William Beaumont Hospital, Royal Oak, MI	Robert Swor	Heather Grace

## List of nonauthor contributors

### SHINE participating sites that enrolled more than 100 patients

**NYP (136)**

**Hub PI:** Jan Claassen

Site	Role	Team Member
NYP Columbia University Medical Center	Principal Investigators	Jan CLAASSEN, Stephan MAYER
	Co-Investigator(s)	Abid QURESHI, Alexander MERKLER, Alexandra REYNOLDS, Ali MAHTA, Andrew BAUERSCHMIDT, Andrew MARTIN, Aws ALAWI, Ayham ALKHACHROUM, Charles ESENWA, Clio A. RUBINOS, David ROH, Elie DANCOUR, Eliza MILLER, Fawaz AL MUFTI, Jeremy RAGLAND, Jiaying (Jayne) ZHANG, Joshua WILLEY, Kara R MELMED, Michael REZNIK, Neal S. PARIKH, Nicholas MORRIS, Sachin AGARWAL, Sara ROSTANSKI, Setareh S OMRAN, Shadi YAGHI, Shivani GHOSHAL, Shouri LAHIRI, Soojin PARK, Teresa MAY, Tim LEKIC, Tomoko KITAGO
	Study Coordinator(s)	Adu MATORY, Angela VELAZQUEZ, Anna CALDERON, Ashley RODRIGUEZ, Caroline COUCH, Cristina FALO, Emma MEYERS, Gregory MATHELIER, Juani FELIZ, Judy LI, Riva LETCHINGER, Sara BRANDT, Stephanie THOMPSON
	Nurse Champion(s)	Philomena JOHN, Rebecca GORDON

**Emory (135)**

**Hub PI:** David W Wright

Site	Role	Team Member
Grady Memorial Hospital	Principal Investigator	Vishal Patel
	Co-Investigator(s)	Aaron ANDERSON, Andrey LIMA, Anika BACKSTER, Anna KATEMA, David W WRIGHT, Fadi NAHAB, Harrison PEARL, Haseeb RAHMAN, Jonathan RATCLIFF, Mahmoud OBIDEEN, Melanie WINNINGHAM, Michael FRANKEL, Minas GEBRU, NICOLE MAHDI, Robin DHARIA, Samir BELAGAJE, SOURABH LAHOTI, Tamara ESPINOZA, Vijayakumar JAVALKAR, Yasir SALEEM,
	Study Coordinator(s)	Alex HALL, Andrea MCDOUGAL, Avou NASSER, DALE DANIEL, Grzegorz DANIELCZOK, Iasson YI, John Paul PAPADOPOULOS, Leah CRAFT, Lovie NEGRIN, MIKE LUNNEY, Natasha MANN, Nick CIARAVELLA, Nick STANLEY, Salim ELHALABY, Stephen HATEZ
	Nurse Champion	Donna BARNETT
Emory University Hospital	Principal Investigator	Vishal Patel
	Co-Investigator(s)	Aaron ANDERSON, Andrey LIMA, Anika BACKSTER, Anna KATEMA, David W WRIGHT, Fadi NAHAB, Harrison PEARL, Haseeb RAHMAN, Jonathan RATCLIFF, Mahmoud OBIDEEN, Melanie WINNINGHAM, Michael FRANKEL, Minas GEBRU,

	Study Coordinator(s)	NICOLE MAHDI, Robin DHARIA, Samir BELAGAJE, SOURABH LAHOTI, Tamara ESPINOZA, Vijayakumar JAVALKAR, Yasir SALEEM, Alex HALL, Andrea MCDOUGAL, Avou NASSER, DALE DANIEL, Grzegorz DANIELCZOK, Iasson YI, John Paul PAPADOPOULOS, Leah CRAFT, Lovie NEGRIN, MIKE LUNNEY, Natasha MANN, Nick CIARAVELLA, Nick STANLEY, Salim ELHALABY, Stephen HATEZ
	Nurse Champion	Mary Grace YBANEZ
Emory University Hospital Midtown	Principal Investigator	Vishal Patel
	Co-Investigator(s)	Aaron ANDERSON, Andrey LIMA, Anika BACKSTER, David W WRIGHT, Fadi NAHAB, Jonathan RATCLIFF, Mahmoud OBIDEEN, Melanie WINNINGHAM, Michael FRANKEL, Minas GEBRU, Robin DHARIA, Samir BELAGAJE, Tamara ESPINOZA, Vijayakumar JAVALKAR
	Study Coordinator(s)	Alex HALL, Andrea MCDOUGAL, Avou NASSER, DALE DANIEL, Iasson YI, Leah CRAFT, Lovie NEGRIN, MIKE LUNNEY, Nick STANLEY, Salim ELHALABY, Stephen HATEZ
	Nurse Champion(s)	Kim LUCAS

**Enrolled 70 – 100 patients**

**Ohio State (79)**      *Hub PI:* Michel Torbey; Diana Greene-Chandos

Site	Role	Team Member
OSU Wexner Medical Center	Principal Investigator	Michel TORBEY, Diana GREENE-CHANDOS
	Co-Investigator(s)	Archana HINDUJA, Deepak GULATI, Jeffrey CATERINO, Yousef HANNAWI, Shraddha MAINALI
	Study Coordinator(s)	Ana Maria GOMEZ RAMIREZ, Areej TARIQ, Mohammad HAMED, Muhammad NASIR, Murat SARI, Nirav PATEL, Sara URIO, Weiping YE
	Nurse Champion	Dorina HARPER
Summa Akron City Hospital	Principal Investigator	Susana BOWLING
	Study Coordinator(s)	Janie WEINHARDT, Kimberly SZYMCZAK (BALLARD), Linette MERCER, Patricia KOCHANOSKI, Rachelle SCHARSU, Robin ROTH, Sara-Jane SALSTROM

**Enrolled 50 – 69 patients**

**Kentucky (54)**      *Hub PI:* Roger Humphries

Site	Role	Team Member
University of Kentucky Hospital	Principal Investigator	Roger HUMPHRIES
	Co-Investigator(s)	Craig CARTER, Creed PETTIGREW, Joel HAMM, Matthew DAWSON, Pamela KOUNS, Peter AKPUNONU, Sameer DESAI, Tammy BRYANT, Terren TROTT
	Study Coordinator(s)	Joann SHORT, Linda DECHTENBERG, Randol BROWN, Theresa MIMS, Debby TAYLOR, Brian DENNIS

**Pittsburgh (53)** *Hub PI:* Cliff Callaway

Site	Role	Team Member
UPMC Presbyterian Hospital	Principal Investigator	Lori SHUTTER
	Co-Investigator(s)	Alexandra WEISSMAN, Ankur DOSHI, Cameron DEZFULIAN, Cliff CALLAWAY, Frank GUYETTE, Jon RITTENBERGER, Jonathan ELMER, Lawrence WECHSLER, Tudor JOVIN
	Study Coordinator(s)	Mary STEFANICK, Sara DIFIORE, Sharon DECESARE, Stacey STULL, Vicki GILCHRIST, Peter ADAMS, Erin GILCHRIST, Erin GRAMM, Megan BUHAY
	Nurse Champion(s)	Melissa CURTIS, Theresa LUCCHITTI
UPMC Mercy Hospital	Principal Investigator	Lori SHUTTER
	Co-Investigator(s)	Christine HAWKES
	Study Coordinator(s)	Janara KOEHLER, Margaret RUSSELL, Michal HAMMOND
	Nurse Champion(s)	Amy SKRITCH, Tammy VOGEL

**UVA (53)**

Site	Role	Team Member
University of Virginia Health System	Principal Investigator	Karen JOHNSTON
	Co-Investigator(s)	Alex DALRYMPLE, Allison CROWELL, Amal ABU LIBDEH, Andrew SCHOMER, Andrew SOUTHERLAND, Bradford WORRALL, Brian SORACE, Christina CHEE, Christopher GROTH, Christopher VACHON, Clark HALEY, Daniel ARTEAGA, Daryl GRESS, David LAPIDES, David MCCOLLUM, David TAPLINGER, Dennis COLE, Derek PYLAND, Elizabeth HUNDT, Erika AXEEN, Erin FOFF, Firas ABDULMAJEED, Greg KUHLMAN, Halley BRIGLIA, James ADDINGTON, Jasmin JO, Jason CROWELL, Jimmy BERTHAUD, Joseph CARRERA, Julie ZHOU, Kathryn NEVEL, Kelsey SATKOWIAK, Kiran KANTH, Lauren MAHONEY, Lauren TALMAN, Liana THEROUX, Lisa TORAN, Madeline CROSS, Margaret BETTIN, Maria DIAZ-ORDONEZ, Mark MCDONALD, Matthew EHRlich, Matthew ELLIOTT, Matthew MCCONNELL, Melanie WARD, Michelle JOHANSEN, Nathaniel BEACHY, Nicole CHIOTA-MCCOLLUM, Nina SOLENSKI, Philip GASTRELL, Prachi MEHNDIRATTA, Rahul GUHA, Reza SEYEDSADJADI, Robert WIGGINS, Robin ULEP, Sarah FREDRICH, Sarah TISEL, Sneha MANTRI, Surabhi RANJAN, Thomas TANDY, Uzoamaka UGOCHUKWU, Vanesa BOTSFORD
	Study Coordinator(s)	Amy FANSLER, Heather HAUGHEY, Sonya GUNTER, Stephanie LOWENHAUPT, Valerie O'DELL, Whitney POLLOCK
	Nurse Champion	Heather TURNER

**UT Houston (51)** *Hub PI:* Elizabeth Jones

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Memorial Hermann Texas Medical Center	Principal Investigator	Elizabeth JONES
	Co-Investigator(s)	Amy NOLAND, Andres BAYONA, Andrew COYNE, Carlos ROLDAN, Caroline BORGAN, Carrie BAKUNAS, Emily ENDACOTT, Ian SMITH, James LEONI, Jason LESNICK, Jason SATTERFIELD, Jonas BEYENE, Joshua GUINDON, Justin SHEPARD, Kasey GILDERSLEEVE, Lindley FOLKERSON, Michael PANDYA, Natalie ELLIOTT, Omar METWALLI, Paulina SERGOT, Pratik DOSHI, Quyen HUYNH, Richard WITKOV, Salvatore VALENTI, Soa-Yih SHER, Stephen HECHT,
	Study Coordinator(s)	Christopher MICHELS, Dinh VUONG, Jonathan NEWSOME, Misty OTTMAN, Monica MOORE, Robert COUCHMAN, Xiuli SUN
	Nurse Champion	Shenequa SOSTAND
Valley Baptist Medical Center	Principal Investigator	Ameer HASSAN
	Co-Investigator(s)	Julio OLMEDA, Wondwossen TEKLE
	Study Coordinator(s)	Olive SANCHEZ, Ivette TORRES, Erlina ABANTAO, Pamela NAUERTH
	Nurse Champion	Kristen E White
Seton Medical Center	Principal Investigators	Jason SHEN, Steven WARACH, Ameer HASSAN
	Co-Investigator(s)	Clifford “Jack” FRAIM, Jeffrey MILEY, John BERTELSON, Kent ELLINGTON, Osvaldo PERURENA, Ray BOGITCH, TJ MILLING
	Study Coordinator(s)	Alison VON EBERSTEIN, Ben HEYEN, Delmas MC BEE, Heidi TYLER, Jessica MORGAN, Laura LACHANCE, Lisa DAVIS, Marianna ALESI, Melissa MIGL
	Nurse Champion(s)	Jonathon HECHT, Phyllis BARRON
Dell Seton Medical Center	Principal Investigators	Jason SHEN, Steven WARACH
	Co-Investigator(s)	Clifford “Jack” FRAIM, Jeffrey MILEY, John BERTELSON, Kent ELLINGTON, Osvaldo PERURENA, Ray BOGITCH, TJ MILLING
	Study Coordinator(s)	Alison VON EBERSTEIN, Ben HEYEN, Delmas MC BEE, Heidi TYLER, Jessica MORGAN, Laura LACHANCE, Lisa DAVIS, Marianna ALESI, Melissa MIGL
	Nurse Champion(s)	Jonathon HECHT, Phyllis BARRON

**Enrolled 30 – 49  
patients**

**Augusta University (47)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Augusta University Medical Center	Principal Investigator	Askiel BRUNO
	Co-Investigator(s)	David HESS, Fenwick NICHOLS, Feroze AFZAL, Hartmut GROSS, Jeffrey SWITZER, Laith MAALI, Mihaela SALER, Nabil WEES, Shannon STEWART, Uttam VERMA
	Study Coordinator(s)	Brian CLOSE, Erin CHRISTENSEN, Kori WILLIAMS, Linda JONES, Natalie BISHOP, Sherif SHAABAN, Sneha JACOB, Tanya MIMS, Tawanna MASSENBERG
	Nurse Champion	Jill WILLIAMS



**Stanford (45)****Hub PI:** James Quinn

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Stanford University	Principal Investigator Co-Investigator(s)	Karen HIRSCH Adam MACLELLAN, Adam RIZVI, Anna FINLEY-CAULFIELD, Basit RAHIM, Catherine LEGAULT, Chitra VENKATASUBRAMANIAN, Christina MIJALSKI, Christopher SOUTHWOOD, Divya PRABHU, Gracia MUI, Gregory ALBERS, Ilanit SPOKOYNY, James QUINN, Jenny TSAI, Kyle HOBBS, Maarten LANSBERG, Marion BUCKWALTER, Michael KE, Neil SCHWARTZ, Nirali VORA, Paul GEORGE, Prashanth KRISHNAMOHAN, Sarah LEE, Soo Young KWON, Sun KIM, Waimei Amy TAI
	Study Coordinator(s)	Anita VISWESWARAN, Carine HO, Christine KELLER, Mohit KOCHAR, Rosen MANN

**Temple (44)****Hub PI:** Nina Gentile

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Temple University Hospital	Principal Investigator Co-Investigator(s)	Nina GENTILE Derek ISENBERG, Guillermo LINARES, Imama NAQVI, Jeff BARRETT, Paul KATZ, Wade DEHNKAMP, Yongwoo KIM
	Study Coordinator(s)	Carl BLANCHARD, Hannah REIMER, Brent FREEMAN, Leticia DOMINGO, Paige PALUMBO, Patricia MCNELIS, Vernon Sayoc KALUGDAN
	Nurse Champion	Suzanne DUROCHER
JFK Medical Center	Principal Investigator Co-Investigator(s)	Mohammad MOUSSAVI Aashish PATEL, Ashish KULHARI, Daniel KORYA, Jaskiran BRAR, Jaward KIRMANI, Siddhart MEHTA, Spozhmy PANEZAI
	Study Coordinator(s) Nurse Champion(s)	Briana DECARVALHO, Charles PORBENI Darilyn PAUL, Gerald GILLEN
	Principal Investigator Co-Investigator(s)	Jacqueline URTECHO Fred RINCON, Jack JALLO, James PEOPLES, Lauren NG, Maria Carissa PINEDA, Matthew VIBBERT, Michelle GARDECKI, Muhammad ATHAR, Rodney BELL
Thomas Jefferson University Hospital	Study Coordinator(s)	Brent FREEMAN, Kara PIGOTT, Meghan-Patirica WAKEFIELD, Melissa WITT, Yvette CRUZ
	Principal Investigator Study Coordinator	Crystal WONG Melissa TIAN

**WVU (36)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
WVU Healthcare Ruby Memorial Hospital	Principal Investigators Co-Investigator(s)	John BRICK, Muhammad ALVI Amelia ADCOCK, Arshi NAZ, Erica BLACKWELL, Jessica PERINI, Martha POWER, Sara DOBRZYNSKI,

Study Coordinator(s) Todd CROCCO, Vicki CHASE  
 Hannah YETZER, Jay SHERMAN, Jennifer DOMICO,  
 Patricia ALTEMUS, Steve DAVIS  
 Nurse Champion(s) Martha POWER, Tanya SMITH

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**UPENN (36)**

**Hub PI:** Jill Baren

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Hospital of the University of Pennsylvania	Principal Investigator	Brett CUCCHIARA
	Co-Investigator(s)	Ali ZANDIEH, Ava LIBERMAN, Cen ZHANG, Christina BLUM, Christopher FAVILLA, Christopher RENNER, Claude NGUYEN, Colin QUINN, Donna KUROWSKI GEORGE, Glenn KONSKY, James SIEGLER, Jean LUCIANO, Jesse THON, Jill BAREN, Judy JIA, Kelley HUMBERT, Kimberly GANNON, Laura STEIN, Michael MCGARVEY, Michael MULLEN, QingYang YUAN, Scott KASNER, Steven MESSE
	Study Coordinator(s)	Andrew LAYNE, Christopher GIBSON, Dana BROWN, Devin KEATING, Erica DAHLMEIER, Gabriel SCHWARTZ, Jason MARSHALL, Joel DURINKA, Katherine (Lamond) BLACKBURN, Mary Elizabeth DESANTO, Melissa YATES, Nichole GALLATTI, Sean SPANGLER, Yohko OGAWA
	Nurse Champion	Jeanie LUCIANO
Abington Memorial Hospital	Principal Investigator	David WEISMAN
	Co-Investigator(s)	Brad KLEIN, Brett CUCCHIARA, Dan GZESH, James COOK, John KHOURY, Lee HARRIS
	Study Coordinator(s)	Allyson BLUE-SCHALLER, Denise GALLAGHER, Jennifer MCGOWAN TRAINER, Katherine (LAMOND) BLACKBURN, Priyahareshni GNANASEKAR
WellSpan York Hospital	Principal Investigator	Brent BECKER
	Co-Investigator(s)	David LEE, Erik KOCHERT, Guy YOUNGBLOOD, Jeremy HUTCHINS, Mark GONZALES, Matthew STEPHENS, Robert STUNTZ, Thomas YEICH, William FIELDS
	Study Coordinator(s)	Barbie STAHLMAN
	Nurse Champion	Teri REBERT

**Wayne State (35)**

**Hub PI:** Robert Welch

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Detroit Receiving Hospital	Principal Investigators	Benjamin ATKINSON, Claire PEARSON, Greg NORRIS, Wazim MOHAMED
	Co-Investigator(s)	Brian O'NEIL, Robert SHERWIN, Robert WELCH, Pratik BHATTACHARYA, Preet VARADE
	Study Coordinator(s)	Alessandra PALAZZOLO, Alexandra DEZIA, Antoine KHOURY, Arslan MAHMOOD, Atika SINGH, Craig MCLENDON, Craig THOMAS, Farhan AYAZ, Jonathon OTTOLINI, Joshua PHILLIP, Justin SABOL, Mitchell HOYER, Patrice WADE, Patrick MEDADO, Payal KAPADIA, Randy KASS-SHAMOUN, Reba JOHN, Robert KAS-SHAMOUN, Saikat BHUIYAN, Samaa RIZK, Samuel CECKOWSKI, Shobi MATHEW, Sydnie BROWN, Syed Imran AYAZ, Theodore FALCON, Thomas MAZZOCCO,
	Nurse Champion	

Valerie MIKA  
Sheri FRANK

Sinai-Grace Hospital	Principal Investigators	Claire PEARSON, Greg NORRIS, Wazim MOHAMED
	Co-Investigator(s)	Brian O'NEIL, Robert SHERWIN, Robert WELCH, Pratik BHATTACHARYA
	Study Coordinator(s)	Alessandra PALAZZOLO, Alexandra (BARANYK) DEZIA, Arslan MAHMOOD, Atika SINGH, Craig MCLENDON, Craig THOMAS, Farhan AYZAZ, Jonathon OTTOLINI, Joshua PHILLIP, Justin SABOL, Mitchell HOYER, Patrick MEDADO, Payal KAPADIA, Randy KASS-SHAMOUN, Reba JOHN, Robert KAS-SHAMOUN, Saikat BHUIYAN, Samaa RIZK, Samuel CECKOWSKI, Shobi MATHEW, Sydnie BROWN, Syed Imran AYZAZ, Theodore FALCON, Thomas MAZZOCCO, Valerie MIKA
William Beaumont Hospital - Troy	Principal Investigator	Aveh BASTANI
	Co-Investigator(s)	Aharon Gedaliah COOPER, Albert ROCCHINI, Brett TODD, David DONALDSON, Matthew CHRISTENSEN, Michael OPSOMMER, Steven DIMSDALE
	Study Coordinator(s)	Blerina POPLE, Heather GRACE, Heonia HILLOCK, Kathleen MAYS-WILSON, Kristen PALOMBA, Megan HAUSLER, Pamela MARSACK, Ryan PATERNOSTER

#### Mayo Clinic (34)

Site	Role	Team Member
Mayo Clinic	Principal Investigator	Kevin BARRETT
	Co-Investigator(s)	Benjamin EIDELMAN, William David FREEMAN, Josephine HUANG, Maisha ROBINSON, James MESCHIA
	Study Coordinator(s)	Alexa RICHIE, Cristin WILLIAMS, Dale GAMBLE, Emily EDWARDS, Jaya VIJAYAN, Sabrina SELMAN, Sothea LUKE, Veronica MUNET-DIAZ
	Nurse Champion	Lesia MOONEY

#### Cincinnati (33) *Hub PI:* Opeolu Adeoye

Site	Role	Team Member
University of Cincinnati Medical Center	Principal Investigator	Opeolu ADEOYE
	Co-Investigator(s)	Adam JASNE, Anna GENSIC, Art PANCIOLI, Brett KISSELA, Brian KATZ, Brian OLOIZIA, Brian STETTLER, Bryan ECKERLE, Daniel KANTER, Daniel WOO, Dawn KLEINDORFER, Elisheva COLEMAN, Erin MCDONOUGH, Jonah GROSSMAN, Jordan BONOMO, Joseph BRODERICK, Julian MACEDO, Katrina PEARISO, Kyle WALSH, Matthew FLAHERTY, Mercedes FALCIGLIA, Michael STAR, Muhammad ZAGHLOULEH, Natalie KREITZER, Pooja KHATRI, Rahul KARAMCHANDANI, Sabreena GILLOW, Sameer SHARMA, Simona FERIOLI, Stacie DEMEL, William KNIGHT
	Study Coordinator(s)	Abigail VOLLMER, Alisha HODGE, Amanda NACIFF-CAMPOS, Anthony SPUZZILLO, Anthony WOLFER, Azeem AHMAD, Cindy CALLIHAN, Danielle CHIN,

Devaughn CRAWFORD, Elizabeth MEYER, Emily GOODALL, Erin BELL, Erin NEEFUS, Hannah VESTER, Hilary PEREZ, Irene EWING, Irene EWING, Jacob LUTZ, Jamey FRASURE, Janice CARROZZELLA, Jessica DEATON, Judith SPILKER, Julie BROCKMAN, Kathleen HARRISON, Kelsey BLAZE, Krista SWEGHEIMER, Laura SYORI, Lauren KEENE, Lauren TERRY, Lena TABBAA, MacKenzie SHIVERS, Maria DODD, Matt MANNION, Michele JASNE, Mikayla VACLAV, Misty WETHINGTON, Mollie MOSLEY, Naila MERCHANT, Nate BRUNTY, Nick LOCAPUTO, Pamela KIMMEL, Pamela SCHMIT, Raechel COOLEY, Samantha KRAMER, Sara KEEGAN, Shannon DEEDS, Steven GAYDA

**Enrolled 10 – 29 patients**

**Utah (29)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
University of Utah Healthcare	Principal Investigator	Jana WOLD
	Co-Investigator(s)	Adam DEHAVENON, Aleks TKACH, Alex LINN, Alicia BENNETT, Brian MARCUS, Chelsea MEYER, Dana DEWITT, Jennifer MAJERSIK, Jerdan RUFF, Lee CHUNG, Muhammad Nabeel CHAUHAN, Peter HANNON, Raymond GRAMS
	Study Coordinator(s)	Crystal NEATE, Joshua LETSINGER, Ka-Ho WONG, Kinga AITKEN, Lilly Siauto FAGATELE, Michael DELA CRUZ, Sara WOLTZ, Stephen CHATWIN, Suyi NIU
	Nurse Champion	Julie MARTINEZ

**SUNY Downstate (24) *Hub PI:* Steven Levine**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Lincoln Medical and Mental Health Center	Principal Investigators	Nicholas CAPUTO, Steven LEVINE, Raghu LOGANATHAN
	Co-Investigator(s)	Balavenkatesh KANNA, Kennedy OMONUWA, Misbahuddin KHAJA, Riyadh BASIR, Shekar MURTHY
	Study Coordinator(s)	Jessica MONTALVO, Martha Ivett KYRIACOU, Colette NGAJURE
	Nurse Champion(s)	Lisa GRIPPO, Margaret PEREIRA
SUNY Downstate Medical Center	Principal Investigator	Steven LEVINE
	Co-Investigator(s)	Adrain MARCHIDANN, Artem SUNIK, Ashika JAIN, Diana ROJAS-SOTO, Helen VALSAMIS, Jennifer MARTINDALE, Lorenzo PALADINO, Qing HAO, Richard JACKSON, Richard SINERT, Shahriar ZEHTABCHI, Susan LAW, Weijun JIN, Yongwoo KIM
	Study Coordinator(s)	Bryce PETTY, Jonathan SINGER, Nadege GILLES, Sarah (ZELONIS) WEINGAST
	Nurse Champion(s)	Mr. EADDY, Ms. WATSON-GREY
Kings County Medical Center	Principal Investigator	Jennifer MARTINDALE, Susan LAW
	Co-Investigator(s)	Steven LEVINE, Ethan BRANDLER, Benedict TAN,

	Study Coordinator(s)	Volodymyr VULKANOV, Pia CHATTERJEE Shreya PANDYA, Bryce PETTY, Jonathan SINGER, Nadege GILLES, Sarah (ZELONIS) WEINGAST
	Nurse Champion	Dorothy SALMON-LINDSAY
Maimonides Medical Center	Principal Investigators	Steven RUDOLPH
	Co-Investigator(s)	Christian FROMM
	Study Coordinator(s)	Alla SHAPIRO, Antonios LIKOUREZOS, Ilyya PUSHKAR, Rukhsana HOSSAIN, Nadege GILLES, Sarah (ZELONIS)
	Nurse Champion(s)	WEINGAST Holly MORHAIM, Marlene ALEXIS-FRANCIS, Yelena ILYASOVA

**Minnesota (19)**      *Hub PI:* Michelle Biros

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Hennepin County Medical Center	Principal Investigator	Ivan MATOS DIAZ, Michelle BIROS, Mustapha EZZEDDINE
	Co-Investigator(s)	Katherine JACOBY, Rwoof RESHI Benjamin MILLER, Christopher STREIB, Daraspreet KAINTH, Divyajot SANDHU, Haralabos ZACHARATOS, Huseyin TORE, Jae KIM, Jamie STARKS, Kenneth SHEA , Laura FOSTER, Mohammed ALKUWAITI, Nathan SIT, Saritha KUNDOOR, Shailesh MALE, Shola ALUKO, Taka HIGASHIMORI
	Study Coordinator(s)	Abbey STAUGAITIS, Amanda WELLER, Audrey HENDRICKSON, Catherine NEWCOMB, Chloe LAWYER, David HILDEBRANDT, Eric JATON, Julie SCHERBER, Justin EKLUND, Kathleen MILLER, Michelle LAMBERT
	Nurse Champion	LAMBERT Josh GRAMLING
University of Minnesota Medical Center	Principal Investigator	Mustapha EZZEDDINE, Rwoof RESHI, Oladi BENTHO
	Co-Investigator(s)	Benjamin MILLER, Christopher STREIB, Daraspreet KAINTH, Divyajot SANDHU, Haralabos ZACHARATOS, Huseyin TORE, Jae KIM, Jamie STARKS, Kalyan SAJJA, Kenneth SHEA, Kristen BARKLOW, Laura FOSTER, Michelle BIROS, Mohammed ALKUWAITI, Nathan SIT, Saritha KUNDOOR, Shailesh MALE, Sherief BOSS, Shola ALUKO, Taka HIGASHIMORI, Tapan MEHTA
	Study Coordinator(s)	Abbey STAUGAITIS, Amanda WELLER, Audrey HENDRICKSON, Catherine NEWCOMB, Chloe LAWYER, David HILDEBRANDT, Eric JATON, Julie SCHERBER, Justin EKLUND, Kathleen MILLER, Michelle LAMBERT
	Nurse Champion	LAMBERT Mary Fran TRACY

**Wisconsin (19)**      *Hub PI:* Tom Aufderheide

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Froedtert Memorial Lutheran Hospital	Principal Investigator	John LYNCH
	Co-Investigator(s)	Marc LAZZARO, Osama ZAIDAT, Paul KNUDSON, Riccardo COLELLA, Tom AUFDERHEIDE, Albert YEE, Ann HELMS, Anne JOHNSON, Cory WILSON, Craig SKOLD, Dennis SHEPHERD, Diane BOOK, Eduardo

	CASTRO, Edward BARTHELL, Gary GERSCHKE, Heidi HARKINS, Howie CROFT, Jeff GLASPY, John WHITCOMB, Jonathan RUBIN, Keith RADER, Mike BRIN, Orlando ALVAREZ, Paul COOGAN, Peter HOLZHAUER, Shekar KURPAD, Steven MOTARJEME, Thomas REMINGA, Vijay JOHNSON, William HASELOW, William KUMPREY
Study Coordinator(s)	Adam DRENT, Alicia CLAUSEL, Amanda EMMRICH, Amy HESSETHALER, Ashley WUERL, Bethany QUERING, Caroline HERDEMAN, Carolyn HEAL, Christopher SANDOVAL, Danielle SPARROW, Denise HALVORSEN, Disha CHHEDA, Geri PRICE, Igli ARAPI, Jacob LABINSKI, Jamie JASTI, Jasmine BALANGUE, Joe BRANDT, Karla HANSEN, Katherine BURPEE, Laura TONYAN, Linda MATTRISCH, Lisa MARTIN, Madeline ZEISSE, Melissa BOETTCHER, Melissa HELM (KNIGHT), Melissa MENA, Mitchell SAUDER, Rachel WEBER, Samantha GAUGER, Sarah ABDALLAH, Sonia MALDONADO-SCHMIDT, Stephanie ZELLNER, Tiffany BOWEN, Tiffany SCHUSTER, Tonia QAISAR, William VON RUEDEN

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**HFHS (18)**      *Hub PI:* Christopher Lewandowski

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Henry Ford Hospital	Principal Investigator	Christopher LEWANDOWSKI, Shaneela MALIK
	Co-Investigator(s)	Angelos KATRAMADOS, Daniel MILLER, Hebah HEFZY, Joseph MILLER, Jumana NAGARWALA, Panayiotis MITSIAS, Raymond FOWKES, Stephan MAYER, Taher VOHRA
	Study Coordinator(s)	Amanda ROBICHAUD, Amjad TARBOOSH, Anne Marie LUNDELL, Christopher PRICE, Jacob ROSS, Jared GOLDBERG, Jo-Ann RAMMAL, John FRANCE, Kaitlin ROSE, Kaleem CHAUDHRY, Kathleen MAYS-WILSON, Melissa ODDO, Meri MUMINOVIC, Randy BITRUS, Richard THOMPSON, Sean-Matthew CALO, Shannen BERRY, Shantel GRIFFIN-REED, Syed RAHMAN, Theresa MCQUAID
	Nurse Champion	Anna SECEN-ULAKOVICH
University of Michigan University Hospital	Principal Investigator	Kyle SHEEHAN
	Co-Investigator(s)	Cemal SOZENER, Craig WILLIAMSON, Darin ZAHURANEC, Devin BROWN, Eric ADELMAN, James BURKE, Lesli SKOLARUS, Lewis MORGENSTERN, Michael-Mei-Hwa WANG, Mollie MCDERMOTT, Natalie WHEELER, Phillip SCOTT, Richard SCHEER, Robert SILBERGLEIT, Venkatakrishna RAJAJEE, Will MEURER, William BARSAN
	Study Coordinator(s)	Heidi ZAYAN, Karen FRISCH, Ron BALL, Sinan HANNA, Tina CHEN
	Nurse Champion(s)	Kim SCHMIDT, Dee MIDDLETON

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**Mt Sinai (17)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
The Mount Sinai Hospital	Principal Investigator	Neha DANGAYACH, Stephan MAYER
	Co-Investigator(s)	Aaron TANSY, Alexandra REYNOLDS, Ali EXXATI, Anil RAMINENI, Cappi LAY, Clara BOYD, Errol GORDON, Gurmeen KAUR, Ivan MATOS DIAZ, Javaad AHMAD, John LIANG, Kaitlin REILLY, Kara SHEINART, Laura STEIN, Mandip DHAMOON, Moshe MIZRAHI, Pavis LAENGVEJKAL, Samson ZARBIV, Stanley TUHRIM, Sypridoula TSETSOU
	Study Coordinator(s)	Chrisitine CRABTREE, Christy CHAN, Danielle WHEELWRIGHT, Glenna LEE, Pradhita MADDIREDDY, Ricardo RENVILL, Stephen GRIFFITHS, Ziya ZHANG
	Nurse Champion(s)	Mignon GUISHARD-POLE, Sonia NELSON

**UCLA (16)**      *Hub PI:* Sidney Starkman

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Ronald Regan UCLA Medical Center	Principal Investigator	Sidney STARKMAN
	Co-Investigator(s)	Adrian BURGOS, Allison ARCH, Anita TIPIRNENI, Arun CHHABRA, Chuan Frances FAN, David LIEBESKIND, Doojin KIM, Jason HINMAN, Jason TARPLEY, Jeffrey SAVER, Josephine HUANG, Konark MALHOTRA, Kunakorn ATCHANEEYASAKUL, Kyle KERN, Latisha SHARMA, Lindsey FRISCHMANN, Lucas RAMIREZ, May NOUR, Melissa REIDER-DEMERS, Mersedeh BAHRHOSSEINI, Michael MCMANUS, Nathan GAINES, Neal RAO, Neil MALUSTE, Parampreet SINGH, Paul VESPA, XianNan TANG, Zuolu LIU
	Study Coordinator(s)	Greg WONG, Ileana GRUNBERG, Janic CHUA, Judy GUZY, Julius WENG, Vivek SINGH
	Nurse Champion	Regina OLIVAS
Long Beach Memorial Medical Center	Principal Investigator	Nima RAMEXAN-ARAB
	Co-Investigator(s)	Banafsheh YAFEH, Maged TANIOS, Michael THOMPSON, Nirav PATEL, Omid MOIDVAR
	Study Coordinator(s)	Angie WEST, Caroline CALLEROS, Dena HOPKINS, Francoise TOUSSANT-JONES, Linda KERR, Marielou KEUTH, Rebecca RABENN, Roxana FLORES
	Nurse Champion	Angie WEST

**Mass General (15)**      *Hub PI:* Joshua Goldstein

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Massachusetts General Hospital	Principal Investigator	Christopher ANDERSON
	Co-Investigator(s)	Abbas KHARAL, Alvin DAS, Anand VENKATRAMAN, Ananda FINE, Andrea HARRIOTT, Andrea MOROTTI, Andreas CHARIDIMOU, Anne-Katrin GIESE, Arne LAUER, Ayaz KHAWAJA, Ayush BATRA, Brian EDLOW, Charlene ONG, Christina MIJALSKI, Daniel RUBIN, David CHUNG, David LERNER, David LIN, Doungporn RUTHIRAGO, Edilberto AMORIM, Eli ZIMMERMAN, Elif GOKCAL, Fadar OTITE, Faheem SHERIFF, Frieder SCHLUNK, Gregoire BOULOUIS, Guido FALCONE, Haitham ALABSI, Jennifer KIM, Jonathan ROSAND, Joshua

GOLDSTEIN, Kelly SLOANE, Lee SCHWAMM, Li XIONG, Marc MALONEY, Marco PASI, Mark ETHERTON, Matthew BEVERS, Ming-Cheih DING, Minjee KIM, Natalia ROST, Navid VALIZADEH, Patricia MUSOLINO, Pedro PINTO, Rajan GADHIA, Ribal BASSIL, Richa SHARMA, Robert REGENHARDT, Saef IZZY, Sahar ZAFAR, Sameen JAFARI, Samuel SNIDER, Sandro MARINI, Sarah NELSON, Sarah WAHLSTER, Sergi RAMIREZ MARTINEZ, Shreyansh SHAH, Shyam RAO, Starane SHEPHERD, Thabele LESLIE-MAZWI, Xuemei CAI, Zachary THRELKELD

Study Coordinator(s) Abigail COHEN, Andrew WARREN, Brittany MILLS, Carissa TUOZZO, Caroline RIZZO, Casey COKKINIAS, Christopher FLYNN, Chun Mei SU, Devin QUALLS, Emily BENSON, Grace RILEY, Greg TIRRELL, Kristen MCNAMARA, Lauren BARTON, Melissa HOWELL, Panos FOTIADIS, Rebecca CLAPHAM, Ryan CALLAHAN, Sarah GRILL, Shane DONNELLY, Thomas GOMES, Zora DIPUCCHIO

Nurse Champion(s) Kathleen MARTIN, Kathryn HALL, Kathleen GRINKE, Vanessa MCKENNA

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Tufts Medical Center	Principal Investigator Co-Investigator(s)	Joshua KORNBLUTH Corey PENTO, David THALER, Deborah GREEN-LAROCHE, Janice MCLAUGHLIN, Julia BIANCO, Lester LEUNG, Shaylin KIRBY, Thomas SCANDURA, Xuemei CAI
	Study Coordinator(s) Nurse Champion	Haley HUGGINS, Lindsey SOLL, Michelle BETTLE, Sarah GANS Corey PENTO

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**Northwestern (14)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Northwestern Memorial Hospital	Principal Investigator Co-Investigator(s)	Shyam PRABHARKARAN Arth SRIVASTAVA, Chen LIN, Fan CAPRIO, Ilana RUFF TREIBER, Jina YOUN, Linda JIANG, Philip CHANG, Rajbeer SANGHA, Richard BERNSTEIN, Scott MENDELSON
	Study Coordinator(s)	Carlos CORADO, Erin WYMORE, Jillian LUX, Shannon STANFILL

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**UTSW (14)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
UT Southwestern Medical Center	Principal Investigator Co-Investigator(s)	Christiana HALL Adam WILLIS, Bethany LUSSIER, Claudia PEREZ, DaiWai OLSON, Julian YANG, Junaid KALIA, Mark JOHNSON, Mohamed OSMAN, Narengia PIERRE-LOUIS, Shraddha MAINALI, Stephen FIGUEROA, Venkatesh AIYAGARI, Zakraus MAHDAVI
	Study Coordinator(s)	Cecila HERNANDEZ, Christopher PALIOTTA, Deanna MYER, Jacob DENEY, Jenny BENITEZ, Katrina VAN DE

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Nurse Champion(s) BRUINHORST, Maria MARTINEZ, Michelle  
 PROVENCHER, Pimen KURASHVILI, Sonja STUTZMAN,  
 Susie MADISON  
 DaiWai OLSON

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**Baylor (11)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Baylor College of Medicine Medical Center	Principal Investigator	Chethan RAO, Jose SUAREZ
	Co-Investigator(s)	Alexandros GEORGIADIS, Benedict TAN, Bilal BUTT, Christos LAZARIDIS, Eric BERSHAD, Kinjal DESAI, Mohamed GAGOEH, Nelson MALDONADO, Pramod GUPTA, Rahul DAMANI, Sanjeev SIVAKUMAR, Stelios SMIRNAKIS, Syed KAZMI
	Study Coordinator(s)	Emily JOBE, Eusebia CALVILLO
	Nurse Champion	Perla LAWRENCE

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**UCSF (11)** *Hub PI:* Claude Hemphill

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
San Francisco General Hospital	Principal Investigator	Claude HEMPHILL
	Co-Investigator(s)	Cathra HALABI, Debbie YI MADHOK, Rene COLORADO, Roger CHENG, Ahmad AHMAD, Anh NGUYEN, Claude HEMPHILL, Elizabeth CAHILL, Natalie CHENG, Neel SINGHAL, Nerissa KO, Nirav SHAH, QingYand YUAN, Shahed TOOSI
	Study Coordinator(s)	Blakely ANDREWS
	Nurse Champion	Christine MARTIN
UCSF Medical Center	Principal Investigator	Wade SMITH
	Co-Investigator(s)	Ahmad AHMAD, Anh NGUYEN, Claude HEMPHILL, Elizabeth CAHILL, Natalie CHENG, Neel SINGHAL, Nerissa KO, Nirav SHAH, QingYand YUAN, Shahed TOOSI
	Study Coordinator(s)	Dominica RANDAZZO, Jeany DUNCAN, Michel MEEKER, Ryan MCCORMICK

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**Enrolled 1 – 9  
patients**

**Maryland (9)** *Hub PI:* Barney Stern

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
University of Maryland Medical Center	Principal Investigator	Marcella WOZNIAK
	Co-Investigator(s)	Barney STERN, Bolanle FAMAKIN, Carolyn CRONIN, Howard EISENBERG, John COLE, Melissa MOTTA, Michael PHIPPS, Steven KITTNER
	Study Coordinator(s)	Amy ROACH, Charlene ALDRICH, Kaitlyn HENRY, Virginia GANLEY
	Nurse Champion	Joseph SUSCO

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**Iowa (9)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
University of Iowa Hospitals and Clinics	Principal Investigator Co-Investigator(s)	Connie PIPER, Kaustubh LIMAYE Ali SHEHARYAR, Allison VOSS, Edgar SAMANIEGO, Emily JAKSICH, Enrique LEIRA, Harold ADAMS, Hyungsub SHIM, Jeffrey MILLER, Laurie GUTMANN, Nandakumar NAGARAJA, Salman AL JERDI, Sami AL KASAB, Santiago ORTEGA-GUITERREZ, Sudeepta DANDAPAT, Waldo GUERRERO
	Study Coordinator(s)	Heena OLALDE, Jeri SIEREN, Nicole KRESSIN

**Arizona (8)**      *Hub PI:* Kurt Denninghoff

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Banner University Medical Center – Tucson Campus	Principal Investigator Co-Investigator(s) Study Coordinator(s)	Kendra DRAKE Chelsea KIDWELL, Kurt DENNINGHOFF Adrienne SHIELDS, Alexia DEMITSAS, Andrew LAINE, Auggie HERBER, Cyndra SCHEU, Derek GIN, Donald DAVIDSON, Ealaf AL RABIA, Eddie SOTO, Elizabeth CAMPBELL, Elizabeth SANGALANG, Eric MOORE, Eva COLLINS , Gary KARTCHNER, Ginny STASINSKI , Isabelle CHEA, Jose CAMARENA, Karen LUTRICK, Kathryn SCHIERLING, Kayla DARRIS, Kristen DEUPREE, Lana BECWAR, Lisa SLAYTON - LOVELAND , Maria GORDON, Mark RAMOS, Matt NELSO , Melisa VAN SKIVER, Michelle NAOUR , Nahid MALEKNIAZI, Nancy HORTON , Noraida BACANI, Ric NAAS, Sara KELLOGG, Steve TRIPONEY, Timothy CARSWELL Joan MACHAMER
	Nurse Champion	

Banner University Medical Center – South Campus	Principal Investigator Co-Investigator(s) Study Coordinator(s)	Kendra DRAKE Kurt DENNINGHOFF Adrienne SHIELDS, Andrew LAINE, Cyndra SCHEU, Donald DAVIDSON, Elizabeth SANGALANG, Eric MOORE, Eva COLLINS, Ginny STASINSKI, Isabelle CHEA, Jose CAMARENA, Karen LUTRICK, Kathryn SCHIERLING, Lana BECWAR, Lisa SLAYTON - LOVELAND, Mark RAMOS, Matt NELSON, Melisa VAN SKIVER, Michelle NAOUR, Nahid MALEKNIAZI, Nancy HORTON, Noraida BACANI, Ric NAAS, Sara KELLOGG, Steve TRIPONEY
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**OHSU (8)**      *Hub PI:* Craig Warden

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Harborview Medical Center	Principal Investigator Co-Investigator(s) Study Coordinator(s)	Craig WARDEN, David TIRSCHWELL Heemun KWOK, Vicki JOHNSON Allison KUNZE, Glenn SCHUBERT, Lela PREWITT, Patricia TANZI, Rizwan KALANI, Thomas-Cole HILLIARD, Wendy HAUGEN, Wesley PLINKE
	Nurse Champion	Pat TANZI

**MedStar (8)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
MedStar Washington Hospital Center	Principal Investigator	Richard BENSON
	Co-Investigator(s)	Alexis SIMPKINS, Amie HSIA, Amjad SHEHADAH, Apoorv PRASAD, Chandni KALARIA, Dennys REYES CANDEDO, John LYNCH, Leigh RICHARD, Nidhi GUPTA, Noorie PEDNEKAR, Saeed ALQAHTANI, Shahram MAJIDI, Syeda NAQVI, Tina BURTON, Claude NOGAY, Travis TAYLOR
	Study Coordinator(s) Nurse Champion(s)	Jamal SMITH, Juby MATHEWS, Leigh DEMONT, Preethy FEIT Karen MORIARTY-POOLE, Shannon BURTON

### Buffalo (6)

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Buffalo General Medical Center	Principal Investigator	Marilou CHING
	Co-Investigator(s)	Amit KANDEL, Christopher DELINE, Eugene GU, Robert SAWYER
	Study Coordinator(s)	Annemarie CRUMLISH, Dawn HOLLER, Navdeep LAIL

### Parkland (6)

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Parkland Hospital	Principal Investigator	Christiana HALL
	Co-Investigator(s)	Adam WILLIS, Bethany LUSSIER, Claudia PEREZ, DaiWai OLSON, Julian YANG, Junaid KALIA, Mark JOHNSON, Mohamed OSMAN, Narengia PIERRE-LOUIS, Shraddha MAINALI, Stephen FIGUEROA, Venkatesh AIYAGARI, Zakraus MAHDAVI
	Study Coordinator(s)	Cecila HERNANDEZ, Christopher PALIOTTA, Deanna MYER, Jacob DENEY, Jenny BENITEZ, Katrina VAN DE BRUINHORST, Maria MARTINEZ, Michelle PROVENCHER, Pimen KURASHVILI, Sonja STUTZMAN, Susie MADISON
	Nurse Champion(s)	Jennifer CROSS, Sondra PEREZ

### Cornell (5)

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
NYP Weill Cornell Medical Center	Principal Investigator	Halinder MANGAT
	Co-Investigator(s)	Adam GANZMAN, Alan SEGAL, Alexander MERKLER, Ali MAHTA, Aws ALAWI, Babak NAVI, Benjamin KUMMER, Dana LEIFER, Daniel LAHM, Dora JAMIESON, David ROH, Elie DANCOUR, Fawaz AL MUFTI, Hooman KAMEL, Jennifer SEVUSH, Jeremy RAGLAND, Michael LERARIO, Micheal REZNIK, Nicholas MORRIS, Shouri LAHIRI, Teresa MAY
	Study Coordinator(s)	Bagovest NIKOLOV, Dana ERGAS, Eric MORRIS, Erica EBER, Ryna MATHIAS
	Nurse Champion	Joyce PHILIP

### OSF (5)

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
OSF St. Francis Medical Center	Principal Investigator Co-Investigator(s) Study Coordinator(s)	Deepak NAIR David WANG, Maureen MATHEWS, Jill Arnold, Judi BECK,

**Penn State (5)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Penn State Hershey Medical Center	Principal Investigator Study Coordinator	Kerstin BETTERMANN Deborah HOFFMAN

**Jackson Memorial (2)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Jackson Memorial Hospital	Principal Investigator Co-Investigator(s)  Study Coordinator(s) Nurse Champion	Maranatha AYODELE Amer MALIK, Erika MARULANDA-LONDONO, Gustavo ORTIZ, Jose ROMANO, Kristine O'PHELAN, Luis F. TORRES, Mohan KOTTAPALLY, Negar ASDAGHI, Nicole SUR, Nirav BHATT, Sebastian KOCH, Sushanth AROOR, Victor DEL BRUTTO, Zeeshan MEMON Andrea ESCOBAR, Avi LANDMAN, Iszet, CAMPO-BUSTILLO Violet KRAMER

**St Thomas (1)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Saint Thomas West Hospital	Principal Investigator Co-Investigator(s) Study Coordinator(s)  Nurse Champion	Frank LAFRANCHISE James GLEMING Alina SIMION, Deb PITTS, Diana COMAN, Kim OWENS, Mitzi BAKER, Nirali SHAH Diana COMAN

**Vanderbilt (1)**

<b>Site</b>	<b>Role</b>	<b>Team Member</b>
Vanderbilt University Hospital	Principal Investigator Co-Investigator(s) Study Coordinator(s)  Nurse Champion	Howard KIRSHNER Lisa HERMANN, Mark BAKER, Michael FROEHLER Andrea REED, Drew ANDERSON, Jessica MARLIN, Matthew WARRICK Diane BROWN

**eTable 1.** Additional baseline and treatment information of the patients

<b>Characteristic</b>	<b>Intensive N=581</b>	<b>Standard N=570</b>
Stroke onset to hospital arrival(h) – median (IQR)	2.7 (1.1-4.8)	2.9 (1.2-5.0)
Hospital arrival to randomization(h) - median (IQR)	3.6 (2.5-5.2)	3.5 (2.4-5.1)
Stroke onset to randomization (h) - median (IQR)	7.1 (4.8-9.4)	7.1 (4.9-9.7)
Randomization to study treatment initiation(h) – median (interquartile range)	1.5 (1.1-2.2)	1.3 (0.9-2.0)
Time on treatment (h) - median (IQR)	71.9 (43.1-72.0)	72.0 (54.0-72.0)
Study treatment completed* – no. (%)	433 (74.5)	510 (89.5)
≥68 hours of study treatment <sup>^</sup>	308 (71.1)	374 (73.3)
Discharged prior to 68 hours	111 (25.6)	126 (24.7)
Withdrawal of care/death	14 (3.2)	10 (2.0)
Study treatment not started – no. (%)	4 (0.7)	5 (0.9)
Reported reasons for study treatment started but not completed – no. (%)	144 (24.8)	55 (9.6)
Patient/Legally authorized representative requests to continue study without study treatment <sup>^</sup>	43 (29.9)	11 (20.0)
Glucose <70 mg/dL x3 within 24hrs <sup>***^</sup>	48 (33.3)	2 (3.6)
Glucose < 40 mg/dL <sup>^</sup>	7 (4.9)	0
Other adverse event/serious adverse event <sup>***</sup>	10 (6.9)	16 (29.1)
Withdrawal of informed consent	3 (2.1)	1 (1.8)
Other <sup>****</sup>	33 (22.9)	25 (45.5)

\*Study treatment completed is defined as at least 68 hours of the 72 hour study treatment or hospital discharge or withdrawal of care/death prior to study treatment completion.

\*\*Stopped study treatment per protocol.

<sup>^</sup>There were a total of 15 patients with glucose values < 40mg/dL. Of the 15, 7 stopped study treatment due to one glucose < 40 mg/dL; 4 stopped early due to 3 glucose <70 mg/dL within 24hrs including at least one <40 mg/dL; 1 Patient/Legally authorized representative requested to continue study without study treatment and had a glucose value below 40mg/dL. The remaining 3 had one glucose value <40 mg/dL yet completed study treatment.

<sup>\*\*\*</sup>Other AEs in the intensive group were: 4 patients with <3 glucose values between 40-70 mg/dL; 5 patients had multiple AEs/SAEs; 1 patient from study treatment due to safety concerns. Other AEs in the standard group were: 7 patients had multiple AEs/SAEs; 1 patient was identified as a type 1 diabetic; 8 patients were hyperglycemic.

<sup>\*\*\*\*</sup>Other reasons included change of diagnosis, hospital unit transfer and lack of IV access.

**eTable 2.** Secondary analyses of primary and secondary outcomes

<b>a. Per Protocol<sup>¶</sup> Analysis</b>						
	<b>Intensive N=530</b>	<b>Standard N=518</b>	<b>Unadjusted Risk Difference (95% CI)</b>	<b>Unadjusted Relative Risk (95% CI)</b>	<b>Adjusted Relative Risk**</b>	<b>P Value ***</b>
<b>Primary Efficacy Outcome at 90 days</b>						
Favorable * modified Rankin Scale - n (%)	107 (20.2)	105 (20.3)	-0.08% (-4.95%, 4.78%)	1.00 (0.78, 1.27)	0.98 (0.87, 1.10)	0.73
<b>Secondary Efficacy Outcomes at 90 days</b>						
Favorable NIHSS (0 or 1) – n/N (%)	138/325 (42.5)	147/344 (42.7)	-0.27% (-7.77%, 7.23%)	0.99 (0.83, 1.18)	1.00 (0.93, 1.09)	0.94
Favorable Barthel Index (95-100) – n/N (%)	251/461 (54.5)	237/443 (53.5)	0.95% (-5.55%, 7.45%)	1.02 (0.90, 1.15)	1.00 (0.95, 1.05)	0.78
SSQOL – n, Median (IQR)	417, 3.73 (2.89,4.39)	401, 3.67 (3.01,4.43)	0.06 (-0.13, 0.25)	-	-	0.69
Severe Hypoglycemia (<40mg/dL) - n (%)	14 (2.6)	0	2.64% (1.28%, 4.01%)	-	-	0.0001
Death- n (%)	54 (10.2)	64 (12.4)	-2.17% (-6.00%, 1.66%)	0.82 (0.59, 1.16)	-	0.27

<sup>¶</sup> Per Protocol is defined as all randomized patients that started treatment, had the 90 day primary outcome, had a final diagnosis of ischemic stroke or TIA, and did not have an eligibility violation.

\*Favorable for the primary efficacy outcome is defined as modified Rankin Scale (mRS) score of 0 in patients with mild stroke (baseline NIHSS 3-7), mRS 0 or 1 in patients with moderate stroke (baseline NIHSS 8-14), and mRS 0, 1 or 2 in patients with severe stroke (baseline NIHSS 15-22) at 90 (-14/+30) days.

\*\* The adjusted analyses were adjusted for baseline stroke severity (NIHSS 3-7 (mild); 8-14 (moderate); 15-22 (severe)) and thrombolysis / thrombectomy use (yes/no).

\*\*\*P values were generated based on the following statistical tests: Wald test for the adjusted analysis of the primary; a chi-square test for the unadjusted binary secondary efficacy and death outcome; Fisher's exact test for the unadjusted binary severe hypoglycemia outcome; a Wilcoxon rank sum test for the unadjusted comparison of SSQOL with reported median and interquartile range (IQR).

<b>b.Primary Analysis when Site is included as a random effect</b>						
	<b>Intensive</b>	<b>Standard</b>	<b>Unadjusted Risk Difference (95% CI)</b>	<b>Unadjusted Relative Risk (95% CI)</b>	<b>Adjusted Relative Risk**</b>	<b>P Value ***</b>
<b>Primary Efficacy Outcome at 90 days</b>						
Primary Analysis	119/581 (20.5)	123/570 (21.6)	-0.83% (-5.72%, 4.06%)	0.96 (0.77, 1.20)	0.93 (0.75, 1.16)	0.53
Per Protocol Analysis	107/530 (20.2)	105/518 (20.3)	-0.08% (-4.95%, 4.78%)	1.00 (0.78, 1.27)	0.96 (0.76,1.21)	0.74

**eTable 3.** Baseline characteristics and treatment information by highest enrolling sites vs all other sites by treatment group

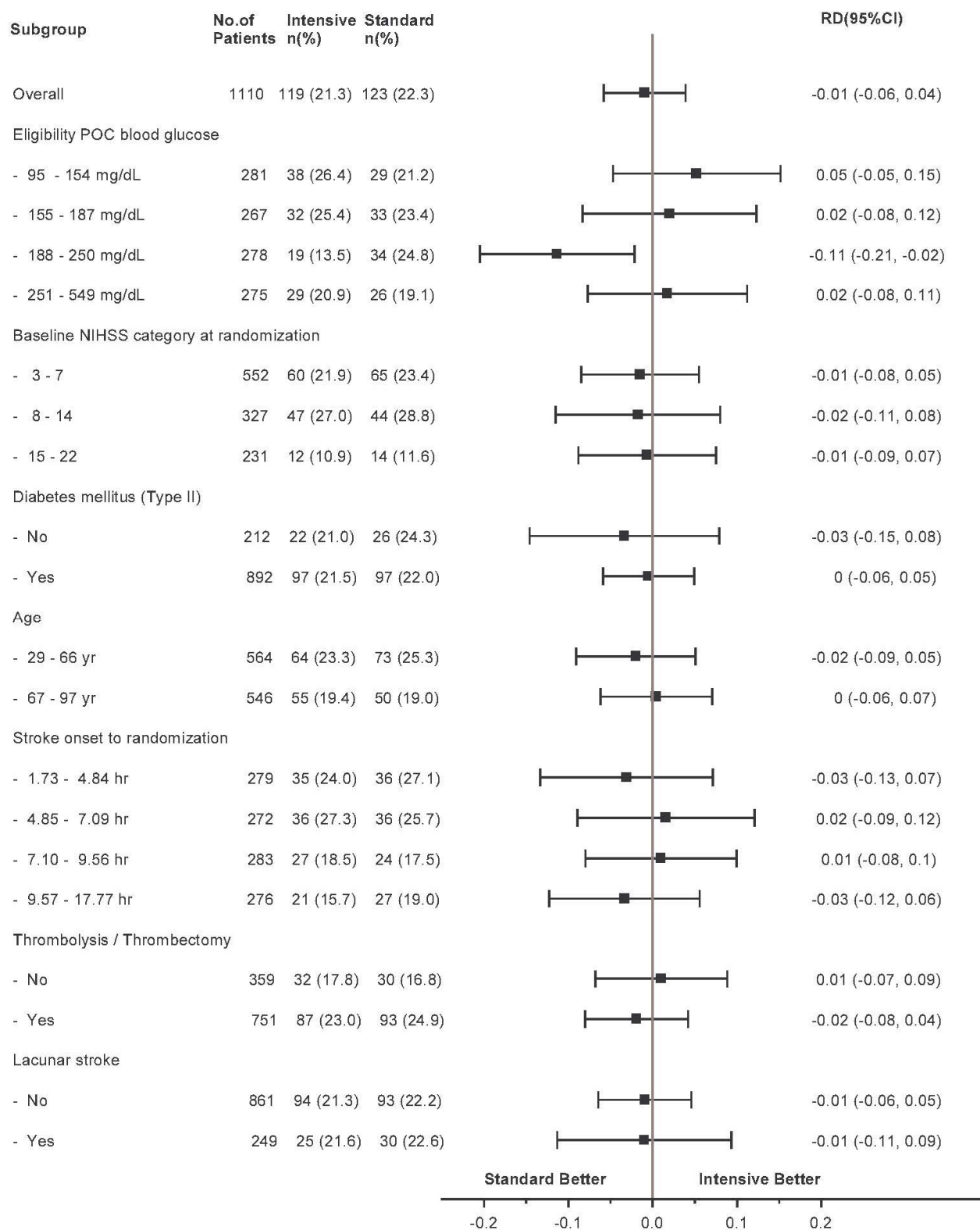
Characteristic	Six Highest Enrolling Sites (>45 enrolled per site)		All Other Sites	
	Intensive (N=243)	Standard (N=242)	Intensive (N=338)	Standard (N=328)
Age (yr) - median (IQR)	65 (57-74)	66 (56-74)	67 (57-76)	65.5 (57-77)
Sex- no. (%)				
Male	130 (53.5)	118 (48.8)	191 (56.5)	188 (57.3)
Female	113 (46.5)	124 (51.2)	147 (43.5)	140 (42.7)
Race - n/N (%)				
White	147/235 (62.6)	154/232 (66.4)	219/325 (67.4)	214/315 (67.9)
Black	85/235 (36.2)	73/232 (31.5)	95/325 (29.2)	81/315 (25.7)
Asian	3/235 (1.3)	4/232 (1.7)	9/325 (2.8)	14/315 (4.4)
Other*	0/235 (0)	1/232 (0.4)	2/325 (0.6)	6/315 (1.9)
Hispanic Ethnicity - n/N (%)	35/239 (14.6)	48/234 (20.5)	52/308 (16.9)	43/306 (14.1)
Final diagnosis - no. (%)				
Ischemic stroke	222 (91.4)	223 (92.1)	320 (94.7)	301 (91.8)
TIA	4 (1.6)	2 (0.8)	4 (1.2)	10 (3.0)
Other	17 (7.0)	17 (7.0)	14 (4.1)	17 (5.2)
Thrombolysis or Thrombectomy** - no. (%)				
Intravenous tPA	150 (61.7)	150 (62)	222 (65.7)	203 (61.9)
Mechanical treatment	36 (14.8)	31 (12.8)	38 (11.2)	41 (12.5)
Intraarterial drug therapy	8 (3.3)	6 (2.5)	6 (1.8)	15 (4.6)
Medical History - no. (%)				
Hypertension	212 (87.2)	214 (88.4)	301 (89.1)	288 (87.8)
Diabetes mellitus (Type II)	201 (82.7)	187 (77.3)	267 (79.0)	268 (81.7)
Hyperlipidemia	141 (58.0)	124 (51.2)	209 (61.8)	203 (61.9)
Coronary artery disease	69 (28.4)	75 (31.0)	90 (26.6)	92 (28.0)
Atrial fibrillation	49 (20.2)	40 (16.5)	75 (22.2)	66 (20.1)
Previous Ischemic stroke	48 (19.8)	38 (15.7)	56 (16.6)	61 (18.6)
Previous large vessel atherosclerosis	15 (6.2)	14 (5.8)	27 (8.0)	25 (7.6)
Eligibility POC Blood Glucose (mg/dL) - median (IQR)	186.5 (154-250)	188.5 (153-242)	188 (153-252)	183 (156-253)
Baseline NIHSS at randomization - median (IQR)	8 (4-12)	8 (5-14)	7 (5-13)	7 (5-12)
NIHSS baseline category at randomization – no. (%)				
NIHSS 3-7	119 (49.0)	114 (47.1)	172 (50.9)	177 (54.0)
NIHSS 8-14	78 (32.1)	70 (28.9)	99 (29.3)	88 (26.8)
NIHSS 15-22	46 (18.9)	58 (24.0)	67 (19.8)	63 (19.2)
Favorable primary efficacy outcome – n/N (%)	56/238 (23.5)	56/234(24.0)	63/320 (20.0)	67/318 (21.1)

IQR – interquartile range; tPA – tissue plasminogen activator; POC – Point of Care; NIHSS – National Institutes of Health Stroke Scale; the NIHSS ranges from 0 to 42, with higher scores indicating greater neurological deficits.

\*Other includes American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander.

\*\*Some patients received more than one type of thrombolysis or thrombectomy.

**eFigure 1.** Primary efficacy outcome, according to subgroups





**eFigure 2.** Relative risk and 95% confidence intervals for reported serious adverse events. Listed by number of patients with at least one event

