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**NN PI:** Lawrence Wechsler, Paula R. Clemens

**NN Coordinator:** Dianne Connors, Christine Amity

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**Site Coordinator:** Dawn Holler

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**NN PI:** Steven Levine, Gil Wolfe

**NN Coordinator:** Annemarie Crumlish

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**Site Coordinator:** Angela Velazquez, Maria Cristina Falo, Gregory Mathelier, Adu Matory

Sachin Agarwal, Fawaz Al-Mufti, Shouri Lahiri, Jeremy Ragland, Shadi Yaghi, Tomoko Kitago, Joshua Willey, Randolph Marshall, David Roh, Alexander E. Merkle, Nicholas Morris, Soojin Park, Teresa May, Sara Rostanski, Tim Lekic, Charles Esenwa, Elie Dancour, Aws Alawi, Michael Reznik, Abid Qureshi, Andrew Martin, Eliza Miller, Alexandra Reynolds, Shivani Ghoshal, Ali Mahta, Juani Feliz, Caroline Couch, Alberto Canaan, Emma Meyers, Stephanie Thompson, Judy Li, Ashley Rodriguez, Sara Brandt, Connie Eng, Biljana Popovic, Michael Schwenk, Marta Scotto, Lucy Liu, Kinara Yang, Donalrey Nieva, Manal Saad, Meral Karakoc

**NN PI:** Karen Marder, Claudia Chiriboga

**NN Coordinator:** Rachel DiLeone, Joyce Moran

### **University of Cincinnati**

**Site PI:** Opeolu Adeoye

**Site Coordinator:** Cynthia Callihan

Joseph Broderick, Bryan Eckerle, Matthew Flaherty, Daniel Kanter, Pooja Khatri, Brett Kissela, Dawn Kleindorfer, Erin McDonough, Arthur Pancioli, Anna Gensic, Brian Stettler, William Knight, Julian Macedo, Natalie Kreitzer, Brian Katz, Stacie Demel, Jordan Bonomo, Rahul Karamchandani, Elisheva Coleman, Michael Star, Kyle Walsh, Jonah Grossman, Brian Oloizia, Aaron Grossman, Simona Ferioli, Adam Jasne, Sabreena Gillow, Katrina Peariso, Misty Wethington, Emily Goodall, Janice Carrozzella, Irene Ewing, Pamela Kimmel, Pamela Schmit, Judith Spilker, Alisha Hodge, Jennifer Powers, Alecia Corcoran, Jamey Frasure, Shannon Iris Deeds, Sara Keegan (Stark), Hilary Perez, Erin Neefus, Erin Bell, Kelsey Blaze, Raechel Cooley, Steven Gayda, Kathleen Harrison, Samantha Kramer, Jacob Lutz, Naila Merchant, Amanda Naciff-Campos, MacKenzie Shivers, Anthony Spuzzillo, Krista Swegheimer, Lauren Terry, Hannah Vester, Judy Houston, Kanyetta Wansley, Amy Dill, Lisa Larson-Altenau, Dorice Smith

**NN PI:** Tracy A. Glauser, Daniel Woo

**NN Coordinator:** Angela Molloy

**Cedars-Sinai Medical Center**

**Site PI:** Shlee S. Song

**Site Coordinator:** Pooja Khanolkar

Konrad H. Schlick, Mani Nezhad, Duy Le, Padmesh S. Rajput, Chang (Peter) Kim, Daniel A. Perez, Annie Yi, Marissa Trester, Eliot Han

**Protocol PI:** Patrick D. Lyden

**University of Utah**

**Site PI:** Peter Hannon

**Site Coordinator:** Crystal Neate

Jennifer Majersik, Jana Wold, Dana DeWitt, Lee Chung, Adam de Havenon, Alicia Bennett, Raymond Grams, Muhammad Chuahan (Nabeel), Alex Linn, Aleksander Tkach, Kinga Aitken, Samuel Sorenson, Maxwell Kilcoyne, Stephen Chatwin, Ka-Ho Wong, Siauto Fagatele (Lilly), Joshua Letsinger, Winter Redd, Bryce Knight, Michele Page

**NN PI:** A. Gordon Smith, Kathryn J. Swoboda

**NN Coordinator:** Richard Whit Coleman, Mariana Duodova, Cathy Revere

**Massachusetts General Hospital (Harvard Partners)**

**Site PI:** Natalia Rost

**Site Coordinator:** Devin Qualls, Abigail Cohen

Christopher Anderson, Charlene Ong, Shyam Rao, Zachary Threlkeld, Jennifer Kim, Faheem Sheriff, Mark Etherton, Ayaz Khawaja, Sameen Jafari (Raza), Rajan Gadhia, Xuemei Cai, Brian Edlow, Guido Falcone, Joshua Goldstein, Leigh Hochberg, Minjee Kim, William Taylor Kimberly, Patricia Musolino, Lee Schwamm, Scott Silverman, Aneesh Singhal, Anand Viswanathan, Frieder Schlunk, Edilberto Amorim, Matthew Bevers, David Chung, Ming-Chieh Ding, Saef Izzy, Sarah Nelson, Shreyansh Shah, Eli Zimmerman, Sahar Zafar, Ayush Batra, Ananda Fine, David Lerner, Starane Shepherd, Christina Mijalski, Andrea Harriott, Guy Rordorf, Lauren Barton, Sergi Martinez-Ramirez, Sandro Marini, Kristin Schwab, Thomas Gomes, Kristen McNamara, Panagiotis Fotiadis, Andreas Charidimou, Li Xiong, Andrea Morotti, Gregoire Boulouis, Gregory Tirrell, Anne-Katrin Giese, Rebecca Clapham, Brittany Mills, Grace Riley, Arne Lauer, Pedro Pinto, Marco Pasi, Samantha Culwell, Alan DiBiasio

**NN PI:** Steven Greenberg

**NN Coordinator:** Sara De Gregorio, Casey Cokkinias

**The Ohio State University Medical Center**

**Site PI:** Archana Hinduja, Michel Torbey

**Site Coordinator:** Muhammed Nasir, Nirav Patel

Diana Greene-Chandos, Andrew Slivka, Mohamad Chmayssani, Shaheryar Hafeez, Deepak Gulati, Courtney Heckman, Laura Buchwalder, Weiping Ye, Ana Maria Gomez Ramirez, Carly Pouttu, Lisa Marmon, Annmarie DiMeo, Lakshmi Phani, Madhuri Somaraju

**NN PI:** John Kissel

**NN Coordinator:** Amy Bartlett

**Barnes-Jewish Hospital (Washington University in St. Louis School of Medicine)**

**Site PI:** Jin-Moo Lee

**Site Coordinator:** Jennifer Babka, Rachel Sargent, Jill Newgent

Andria Ford, Derek Holder, Christian Burrell, Laura Heitsch, Peter Panagos, Colin Derdeyn, Tobias Kulik, Hesham Allam, Javon Edgcombe, David Curfman, Heather Triplett, Kristopher Bakos, Kathryn Vehe

**NN PI:** David B. Clifford

**NN Coordinator:** Mengesha Teshome, Johanna Hartlein

**University of Rochester Medical Center**

**Site PI:** Curtis Benesch

**Site Coordinator:** Ann Leonhardt

Todd Holmquist, Adam Kelly, Bogachan Sahin, Michael Chilungu, Jeffrey Burdett, Sara Dalton, Heather Finley, Dawn Martin, Anthony Noto, Fulvio Roberto (Rob) Gil, Jennifer Richard, Eugene Scharf, Justin Chandler, Ania Busza, Christine Boerman, Stephen Bean, Carol Cole

**NN PI:** Robert Holloway, Jonathan W. Mink

**NN Coordinator:** Christine Annis

**University of Kansas Medical Center**

**Site PI:** Michael Rippee, Marilyn Rymer

**Site Coordinator:** Alison L. Boydston

Colleen Lechtenberg, Yunxia Wang, Craig Shipley, Rawan Albadareen, Lee Rosterman, Barbara Couldry, Leslie Curtis, Rocio Lager, Kristen Filby, Mia Hard, Cory Bivona

**NN PI:** Richard Barohn

**NN Coordinator:** Laura Herbelin, Maureen Walsh, Chad Parks

**Vanderbilt University**

**Site PI:** Michael T. Froehler

**Site Coordinator:** Jessica Sparks Marlin, Diane Brown

Howard Kirschner, Mark Baker, Matt Warrick, Andrea Reed, Jessica Collins, Richard Malone

**NN PI:** Beth Malow

**NN Coordinator:** Karen Adkins, Kelly Lowen

**University of Virginia – Charlottesville**

**Site PI:** E. Clarke Haley

**Site Coordinator:** Stephanie Lowenhaupt

Bradford Worrall, Karen Johnston, Nina Solenski, Andrew Southerland, Christina Chee, Prachi Mehndiratta, Andrew Schomer, David Taplinger, Melanie Ward, Matthew Ehrlich, Matthew Elliot, Christopher Groth, Sneha Mantri, Kathryn Nevel (Stevens), Lisa Toran, Nicole Chiota-McCollum, David

Lapides, Kiran Kanth, Jason Crowell, Halley Briglia, Jimmy Berthaud, Joseph Carrera, Colleen Harman, Valerie Odell, Sonya Gunter, Amy Adams, Kara Parsons

**NN PI:** E. Clarke Haley, C. Ted Burns, Mark Quigg

**NN Coordinator:** Stephanie Lowenhaupt

**Northwestern Memorial Hospital**

**Site PI:** Shyam Prabhakaran

**Site Coordinator:** Carlos Corado

Ilana Ruff, Jillian Lux, Jane Regalado, Krista Carlson

**NN PI:** Tanya Simuni

**NN Coordinator:** Michael Berman, Toi Thompson, Carlos Corado

**Parkland Health & Hospital System (University of Texas Southwestern Medical Center)**

**Site PI:** Mark Johnson

**Site Coordinator:** Jan Cameron-Watts

Alejandro Magadan, Chirantan Banerjee, Ty Shang, William Thayer, Lynda Godowic, Azadeh Mozaffari

**NN PI:** Mark Goldberg

**NN Coordinator:** Mariam Andersen

## Appendix 2 - Adverse Events by System Organ Class and Treatment Group

Column 1	2	3	4	5	6	7	8	9
System Organ Class	Group						RR (95% CI)	p-value
	Treatment N = 66			Placebo N = 44				
	# (%) of Subjects	# of Events	Rate	# (%) of Subjects	# of Events	Rate		
<b>Blood</b>								
Anaemia	15 (22.7%)	16	.085	7 (15.9%)	7	.060	1.43 (0.63, 3.22)	0.4693
Leukocytosis	6 (9.1%)	6	.032	7 (15.9%)	7	.060	0.57 (0.21, 1.59)	0.3679
Lymphadenopathy	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Thrombocytopenia	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Cardiac</b>								
Acute myocardial infarction	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Atrial fibrillation	8 (12.1%)	9	.048	6 (13.6%)	6	.051	0.89 (0.33, 2.39)	1.0000
Bradycardia	1 (1.5%)	1	.005	6 (13.6%)	6	.051	0.11 (0.01, 0.89)	0.0158
Cardiac arrest	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Cardiac failure congestive	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Intracardiac thrombus	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Mitral valve incompetence	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Myocardial infarction	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Pericarditis	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Sinus bradycardia	0 (0%)	0	.000	4 (9.1%)	4	.034	N/A	N/A
Sinus tachycardia	3 (4.5%)	3	.016	1 (2.3%)	1	.009	2.00 (0.21, 18.62)	0.6485
Supraventricular extrasystoles	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Supraventricular tachycardia	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Tachycardia	3 (4.5%)	3	.016	1 (2.3%)	1	.009	2.00 (0.21, 18.62)	0.6485
<b>Eye</b>								
Periorbital oedema	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Gastrointestinal</b>								
Abdominal distension	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Constipation	6 (9.1%)	6	.032	4 (9.1%)	4	.034	1.00 (0.30, 3.34)	1.0000
Diarrhoea	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Duodenal ulcer haemorrhage	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Dyspepsia	2 (3.0%)	2	.011	1 (2.3%)	1	.009	1.33 (0.12, 14.26)	1.0000
Gastrointestinal haemorrhage	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Nausea	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Retroperitoneal haematoma	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Vomiting	0 (0%)	0	.000	4 (9.1%)	4	.034	N/A	N/A
<b>General</b>								
Catheter site phlebitis	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Chest pain	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Face oedema	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Infusion site pain	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A

Injection site pain	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Oedema peripheral	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Pain	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Pyrexia	4 (6.1%)	4	.021	4 (9.1%)	4	.034	0.67 (0.18, 2.53)	0.7111
Vessel puncture site haematoma	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Infections</b>								
Catheter site cellulitis	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Cellulitis orbital	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Groin infection	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Injection site cellulitis	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Pneumonia	1 (1.5%)	1	.005	3 (6.8%)	3	.026	0.22 (0.02, 2.07)	0.2998
Septic shock	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Sinusitis	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Staphylococcal infection	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Urinary tract infection	10 (15.2%)	10	.053	8 (18.2%)	8	.068	0.83 (0.36, 1.95)	0.7936
Urosepsis	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
<b>Injury, Poisoning, and Procedural Comp.</b>								
Contusion	3 (4.5%)	3	.016	3 (6.8%)	3	.026	0.67 (0.14, 3.15)	0.6817
Laceration	1 (1.5%)	2	.011	0 (0%)	0	.000	N/A	N/A
Post procedural haematoma	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Procedural pain	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Wound secretion	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Investigations</b>								
Activated partial thromboplastin time prolonged	4 (6.1%)	4	.021	2 (4.5%)	2	.017	1.33 (0.26, 6.97)	1.0000
Activated partial thromboplastin time shortened	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Aspartate aminotransferase increased	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Blood bilirubin increased	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Blood calcium decreased	5 (7.6%)	5	.027	1 (2.3%)	1	.009	3.33 (0.40, 27.57)	0.3987
Blood chloride increased	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Blood fibrinogen decreased	6 (9.1%)	6	.032	5 (11.4%)	5	.043	0.80 (0.26, 2.46)	0.7520
Blood fibrinogen increased	2 (3.0%)	2	.011	1 (2.3%)	1	.009	1.33 (0.12, 14.26)	1.0000
Blood glucose increased	4 (6.1%)	4	.021	2 (4.5%)	2	.017	1.33 (0.26, 6.97)	1.0000
Blood homocysteine increased	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Blood magnesium decreased	3 (4.5%)	3	.016	0 (0%)	0	.000	N/A	N/A
Blood potassium decreased	4 (6.1%)	4	.021	0 (0%)	0	.000	N/A	N/A
Blood sodium decreased	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
Blood sodium increased	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
C-reactive protein increased	0 (0%)	0	.000	2 (4.5%)	2	.017	N/A	N/A
Ejection fraction decreased	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
Hepatic enzyme increased	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Lymphocyte count decreased	4 (6.1%)	4	.021	4 (9.1%)	4	.034	0.67 (0.18, 2.53)	0.7111
Occult blood positive	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Platelet count decreased	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A

Prothrombin time prolonged	5 (7.6%)	5	.027	6 (13.6%)	6	.051	0.56 (0.18, 1.71)	0.3422
Troponin increased	4 (6.1%)	4	.021	0 (0%)	0	.000	N/A	N/A
Urine output decreased	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
White blood cell count increased	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Metabolic</b>								
Alkalosis	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Gout	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Hyperglycaemia	2 (3.0%)	2	.011	2 (4.5%)	2	.017	0.67 (0.10, 4.56)	1.0000
Hyperlipidaemia	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Hypoalbuminaemia	4 (6.1%)	4	.021	1 (2.3%)	1	.009	2.67 (0.31, 23.07)	0.6463
Hypocalcaemia	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Hypophosphataemia	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
Hypoproteinaemia	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Musculoskeletal</b>								
Arthralgia	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Back pain	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Muscle spasms	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
Musculoskeletal pain	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Neck pain	3 (4.5%)	3	.016	0 (0%)	0	.000	N/A	N/A
Pain in extremity	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Nervous System</b>								
Balance disorder	0 (0%)	0	.000	1 (2.3%)	2	.017	N/A	N/A
Brain oedema	6 (9.1%)	6	.032	4 (9.1%)	4	.034	1.00 (0.30, 3.34)	1.0000
Carotid artery dissection	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Carotid artery stenosis	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Central pain syndrome	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Cerebral haemorrhage	5 (7.6%)	5	.027	2 (4.5%)	2	.017	1.67 (0.34, 8.21)	0.7000
Cerebrovascular accident	7 (10.6%)	10	.053	3 (6.8%)	3	.026	1.56 (0.42, 5.69)	0.7370
Convulsion	3 (4.5%)	3	.016	1 (2.3%)	2	.017	2.00 (0.21, 18.62)	0.6485
Haemorrhage intracranial	15 (22.7%)	15	.080	17 (38.6%)	17	.145	0.59 (0.33, 1.05)	0.0881
Haemorrhagic cerebral infarction	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Headache	12 (18.2%)	16	.085	10 (22.7%)	13	.111	0.80 (0.38, 1.69)	0.6296
Somnolence	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Stroke in evolution	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
<b>Psychiatric</b>								
Agitation	0 (0%)	0	.000	5 (11.4%)	5	.043	N/A	N/A
Confusional state	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Delirium	0 (0%)	0	.000	2 (4.5%)	2	.017	N/A	N/A
Depression	2 (3.0%)	2	.011	1 (2.3%)	1	.009	1.33 (0.12, 14.26)	1.0000
Insomnia	3 (4.5%)	3	.016	0 (0%)	0	.000	N/A	N/A
<b>Renal</b>								
Haematuria	3 (4.5%)	3	.016	4 (9.1%)	4	.034	0.50 (0.12, 2.13)	0.4344
Renal failure acute	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Urinary retention	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Respiratory</b>								
Acute respiratory failure	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000

Bronchospasm	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Cough	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Hypoxia	2 (3.0%)	2	.011	1 (2.3%)	1	.009	1.33 (0.12, 14.26)	1.0000
Oropharyngeal pain	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
Pneumonia aspiration	2 (3.0%)	2	.011	1 (2.3%)	1	.009	1.33 (0.12, 14.26)	1.0000
Pneumothorax	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Productive cough	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Pulmonary embolism	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Pulmonary oedema	1 (1.5%)	1	.005	3 (6.8%)	3	.026	0.22 (0.02, 2.07)	0.2998
Respiratory distress	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
Respiratory failure	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
<b>Skin</b>								
Rash	2 (3.0%)	2	.011	0 (0%)	0	.000	N/A	N/A
<b>Surgical and Medical Proc.</b>								
Aneurysm repair	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
<b>Vascular</b>								
Deep vein thrombosis	1 (1.5%)	1	.005	1 (2.3%)	1	.009	0.67 (0.04, 10.38)	1.0000
Flushing	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Hot flush	0 (0%)	0	.000	1 (2.3%)	1	.009	N/A	N/A
Hypertension	4 (6.1%)	4	.021	1 (2.3%)	1	.009	2.67 (0.31, 23.07)	0.6463
Hypotension	4 (6.1%)	4	.021	6 (13.6%)	6	.051	0.44 (0.13, 1.48)	0.1943
Peripheral ischaemia	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
Phlebitis superficial	1 (1.5%)	1	.005	0 (0%)	0	.000	N/A	N/A
<b>Total</b>	<b>56 (84.8%)</b>	<b>268</b>	<b>1.42</b>	<b>41 (93.2%)</b>	<b>180</b>	<b>1.53</b>	<b>0.91 (0.80, 1.04)</b>	<b>0.2366</b>

Report Generated on Data Submitted and Coded as of: 18Jan2017.

Column Definitions:

1: System Organ Class of AE

2,5: Number and percentage of subjects who have ever had AE

3,6: Total number of AEs; includes multiple AEs of same type per subject

4,7: Number of AEs per 30 days

8: Relative Risk (Treatment relative to Placebo) and 95% confidence interval

9: p-value



## Appendix 3: Serious Adverse Events

Event	3K3A-APC		Placebo		RR (95% CI)	P value
	N (%) Subjects	N Events	N (%) Subjects	N Events		
Total	30 (45.5%)	56	18 (40.9%)	34	1.11 (0.71, 1.73)	0.6971
Cerebrovascular accident	5 (7.6%)	7	3 (6.8%)	3	1.11 (0.28, 4.41)	1
Atrial fibrillation	5 (7.6%)	6	4 (9.1%)	4	0.83 (0.24, 2.93)	1
Brain oedema	5 (7.6%)	5	3 (6.8%)	3	1.11 (0.28, 4.41)	1
Blood fibrinogen decreased	3 (4.5%)	3	1 (2.3%)	1	2.00 (0.21, 18.62)	0.6485
Cerebral haemorrhage	3 (4.5%)	3	2 (4.5%)	2	1.00 (0.17, 5.74)	1
Anaemia	2 (3.0%)	2	1 (2.3%)	1	1.33 (0.12, 14.26)	1
Convulsion	2 (3.0%)	2	1 (2.3%)	1	1.33 (0.12, 14.26)	1
Pneumonia aspiration	2 (3.0%)	2	1 (2.3%)	1	1.33 (0.12, 14.26)	1
Respiratory failure	2 (3.0%)	2	0 (0%)	0	N/A	N/A
Cardiac arrest	1 (1.5%)	1	1 (2.3%)	1	0.67 (0.04, 10.38)	1
Cardiac failure congestive	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Intracardiac thrombus	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Myocardial infarction	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Pericarditis	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Duodenal ulcer haemorrhage	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Retroperitoneal haematoma	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Chest pain	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Septic shock	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Staphylococcal infection	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Blood potassium decreased	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Blood sodium increased	1 (1.5%)	1	0 (0%)	0	N/A	N/A

Ejection fraction decreased	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Hepatic enzyme increased	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Lymphocyte count decreased	1 (1.5%)	1	1 (2.3%)	1	0.67 (0.04, 10.38)	1
Troponin increased	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Carotid artery stenosis	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Haemorrhage intracranial	1 (1.5%)	1	1 (2.3%)	1	0.67 (0.04, 10.38)	1
Acute respiratory failure	1 (1.5%)	1	1 (2.3%)	1	0.67 (0.04, 10.38)	1
Bronchospasm	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Pulmonary oedema	1 (1.5%)	1	1 (2.3%)	1	0.67 (0.04, 10.38)	1
Respiratory distress	1 (1.5%)	1	0 (0%)	0	N/A	N/A
Deep vein thrombosis	1 (1.5%)	1	1 (2.3%)	1	0.67 (0.04, 10.38)	1
Hypotension	1 (1.5%)	1	3 (6.8%)	3	0.22 (0.02, 2.07)	0.2998
Leukocytosis	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Bradycardia	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Pneumonia	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Urosepsis	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Blood glucose increased	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Agitation	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Pneumothorax	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Pulmonary embolism	0 (0%)	0	1 (2.3%)	1	N/A	N/A
Aneurysm repair	0 (0%)	0	1 (2.3%)	1	N/A	N/A