

SUPPLEMENTAL MATERIAL

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Maria Magdalena Alvarado-Garcia; Ira Dauber / Susan Derbyshire; Suhail Zavarro / Aolani
Miller; Kevin Sharkey / Alanza Ferguson; Kirkwood Adams / Jana Glotzer; Jose A Perez / Jodie
Addington; Zulfiquar Bhatti / Carla Burton; Mike B. Melucci / Susan Meier; Michael Huber /
Fujiko Anazawa; Jenica Upshaw / Katelyn Carr; Mark Jeffrey Holmberg / Lois S. Rasmussen;
Vanessa J Lucarella / Kathleen Maloney; Kenneth C. Sabatino / Kathleen Maloney; John
Everett / Emily Kelley; Sandhya Murthy / Angeline Camillo; Nancy Sweitzer / Cindy Schrag;
Peter E. Carson / Jacqueline Gannuscio; Neil Pendril Lewis / Krista Chafin; Alan Bruce Miller /
Erin Richardson; Usman Qayyum / Paige Brown; Dinesh Singal / Danielle Giunta; Arun
Krishnamoorthy / Reema Vallabh; Andrew J Keller / Stephanie Burton; Alexander Adler / Dean
Thompson; Josef Stehlik / Jennifer Hong; Gary J. Luckasen / Scott Kaczowski; Wayne Old /
Melinda Bullivant; John Boehmer / Kevin Gardner; Dinesh K. Gupta / Tammy Davey; Hirsch
Mehta / Gina Ciezkowski; Michael Hong / Elizabeth Hejna; Ashrith Guha / Marcos De Oliveira;
Tariq Haddad / Deanna Overbeck; Hamid Taheri / Abbey Elie; Ioana Dumitru / Ricardo Guedes;
Alain Heroux / Carol Kartje; Marcel E. Zughaib / Candice Edillo; Chad Link / Jennifer Boak;
Andrew Darlington / Kathryn Kaszonyi; Stephen B. Sloan / Deborah Wood; Mayar Jundi / Ann
Ostrander; Sandeep Khosla / Sudha Lukka; Marcus L. Williams / Kimberly Michel; Andre Artis /
Kimberly Armstrong; Nicholas Kondo / Gretchen Kostedt; Israel Galtes / Yasnhai Diaz; Luis

Martinez / Beatriz Penafiel; Jose F. Cardona / Abril Juarez; Shuaib Abdullah / Amy Atwell; Albert J. Sharf / Leonardo Cortes; Ravi Bhagwat / Donna Winterrowd; Elie Michael Donath / Maria Ycaza; Alonzo Jones / Carla Burton; Eve Gillespie / Pat Keane-Richmond; Richard Becker / Rachel Mardis; Peter S. Fail / Vicky Parfait; Siby Ayalloore / Tessie Rideaux; Wade May / Julie Zannini; Atul R. Chugh / Stephanie Alford; Mohsin Alhaddad / Lani Holman; Russell J. Strader / Alicia Gneiting; Terry Wells / Jessica Smith; Vernon Young / Cynthia Buchanan; Ish K Singla / Justin Roth; Henry Ooi / Laura Diedrich; Harry T. Colfer / Denise Antonishen; Michael Bauer / Melissa Galindo; Leslie W. Miller / Delia Johnson; Saul Schaefer / Kevin Chun; Denise Barnard / Matt Kawahara; Brian A. Foley / Sabrina Forbus; Andrey Espinoza / Robin Enea; Enrique Flores / Lorie Benedict; Maria Rosa Costanzo / Josilyn Klimek; Dawn Lombardo / Wei Zhou; Charles Treasure II / Doreen Nicely; David Kraus / Paula Higdon; Van Q Nguyen / Shari Cook.

Table S1. Discontinuation Rate by Randomized Treatment and Safety Event Occurrence.

	Vericiguat	Placebo	Overall
	(N=2519)	(N=2515)	(N=5034)
Syncope or Symptomatic Hypotension			
Censor	492/2207 (22.3%)	466/2248 (20.7%)	958/4455 (21.5%)
Event	122/312 (39.1%)	102/267 (38.2%)	224/579 (38.7%)
Symptomatic Hypotension			
Censor	522/2290 (22.8%)	489/2317 (21.1%)	1011/4607 (21.9%)
Event	92/229 (40.2%)	79/198 (39.9%)	171/427 (40.0%)

Numerators are the number of patients who discontinued treatment. Denominators are the number of patients in each treatment arm, who either experienced the specific safety event or were censored. There were 744 participants with discontinuation due to death, who were excluded from these numbers.

Table S2. Treatment effect on time to symptomatic hypotension or syncope by NT-proBNP subgroups.

Safety outcome	Vericiguat	Placebo	HR (95% CI)	P-value
	Rate (Events)	Rate (Events)		
Symptomatic hypotension or syncope				
NT-proBNP \geq 4000 pg/mL	13.18 (97)	12.28 (90)	1.08 (0.81–1.43)	0.386
NT-proBNP <4000 pg/mL	12.03 (202)	9.61 (161)	1.26 (1.02–1.55)	
NT-proBNP \geq 8000 pg/mL	12.92 (33)	15.69 (39)	0.83 (0.52–1.32)	0.102
NT-proBNP <8000 pg/mL	12.32 (266)	9.82 (212)	1.26 (1.05–1.51)	
Symptomatic hypotension				
NT-proBNP \geq 4000 pg/mL	9.17 (69)	9.19 (68)	1.00 (0.72–1.40)	0.241
NT-proBNP <4000 pg/mL	8.66 (149)	6.78 (116)	1.29 (1.01–1.64)	
NT-proBNP \geq 8000 pg/mL	9.66 (25)	12.37 (31)	0.79 (0.47–1.34)	0.108
NT-proBNP <8000 pg/mL	8.71 (193)	6.95 (153)	1.26 (1.02–1.56)	
Syncope				
NT-proBNP \geq 4000 pg/mL	4.39 (34)	3.64 (28)	1.22 (0.74–2.00)	0.884
NT-proBNP <4000 pg/mL	3.60 (64)	3.11 (55)	1.16 (0.81–1.66)	
NT-proBNP \geq 8000 pg/mL	3.75 (10)	4.97 (13)	0.76 (0.33–1.73)	0.263
NT-proBNP <8000 pg/mL	3.85 (88)	3.07 (70)	1.26 (0.92–1.72)	

CI, confidence interval; HR, hazard ratio; NT-proBNP, N-terminal-pro hormone B-type natriuretic peptide.

Table S3. Treatment effect on time to symptomatic hypotension or syncope by baseline use of SGLT2i.

	Vericiguat	Placebo		
Symptomatic hypotension or syncope	Rate (Events)	Rate (Events)	HR (95% CI)	P-value
No use of SGLT-2 inhibitors	12.16 (300)	10.34 (257)	1.18 (1.00–1.39)	0.792
Use of SGLT-2 inhibitors	22.66 (12)	17.94 (10)	1.32 (0.57–3.06)	

CI, confidence interval; HR, hazard ratio; SGLT-2 , sodium-glucose Cotransporter-2.

Figure S1. Distribution of baseline SBP in VICTORIA.

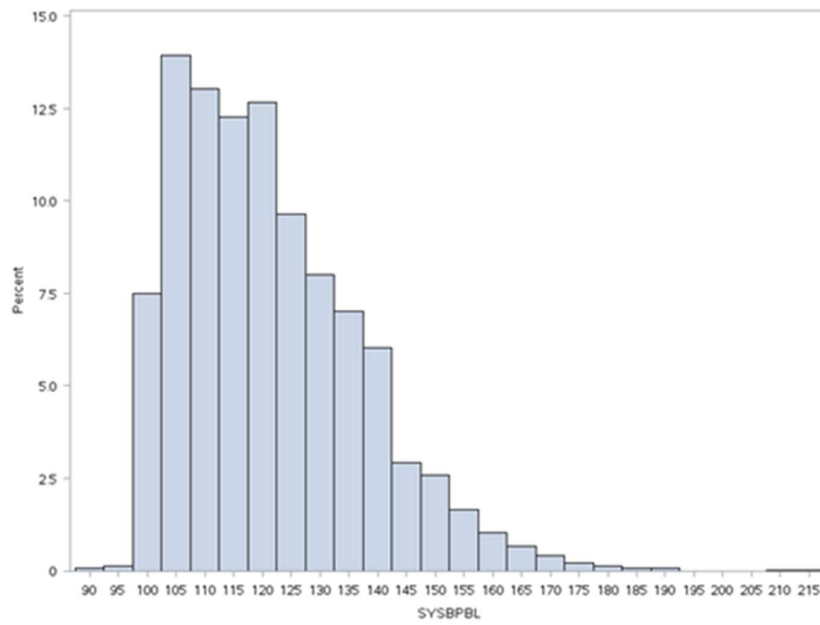


Figure S2. Systolic blood pressure (SBP) trajectory over time by age strata (A) above and below 65 years old, (B) 75 years old, and (C) 85 years old.

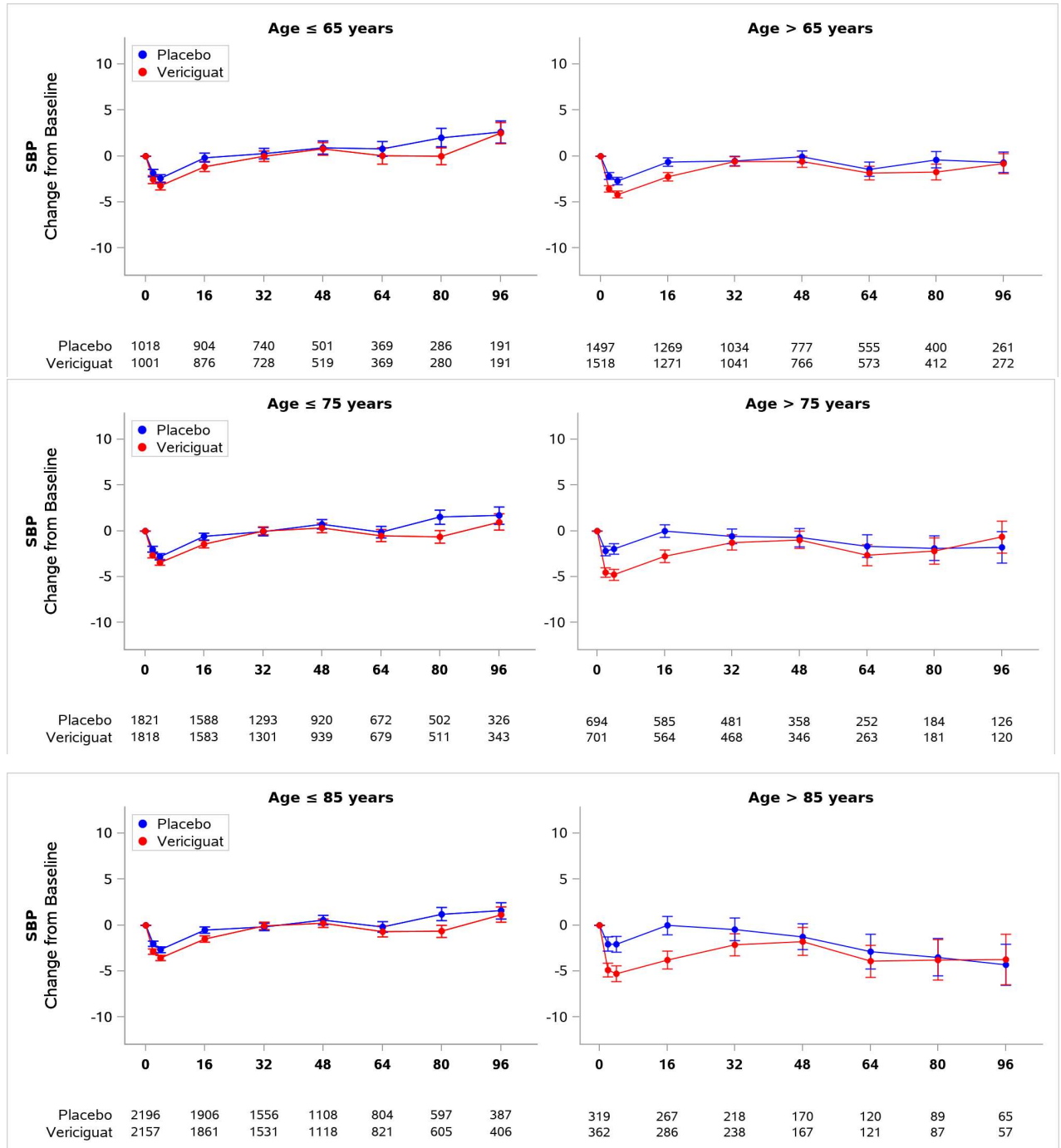


Figure S3. Systolic blood pressure (SBP) trajectory over time in patients receiving (vs not receiving) (A) any renin angiotension system inhibitor (RAS), (B) maximal dose of RAS, and (C) triple therapy (RAS, beta-blocker and mineralocorticoid receptor antagonist) at baseline

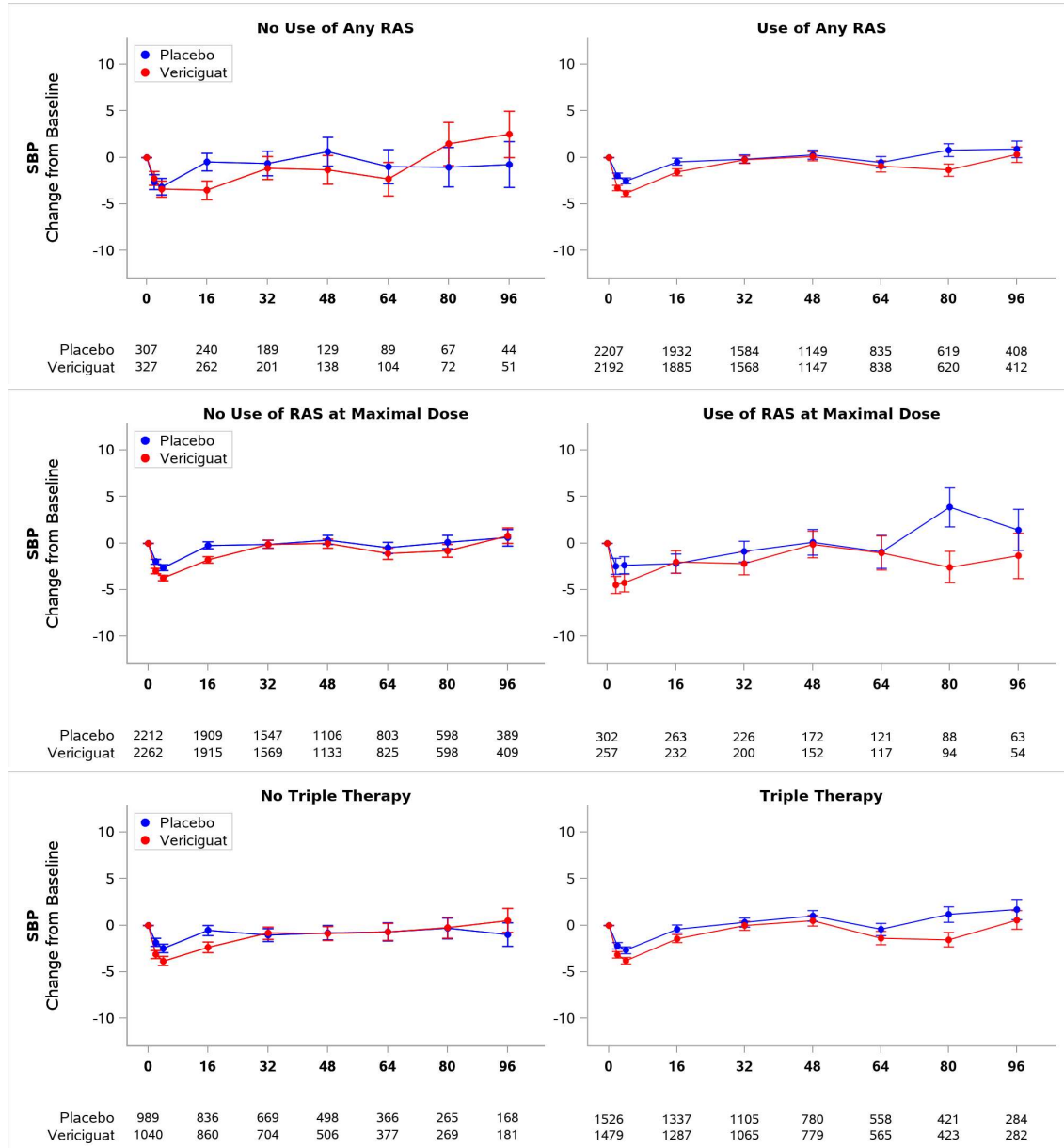


Figure S4. Systolic blood pressure (SBP) trajectory over time in patients with baseline NT-proBNP above and below 4000 pg/mL and 8000 pg/mL

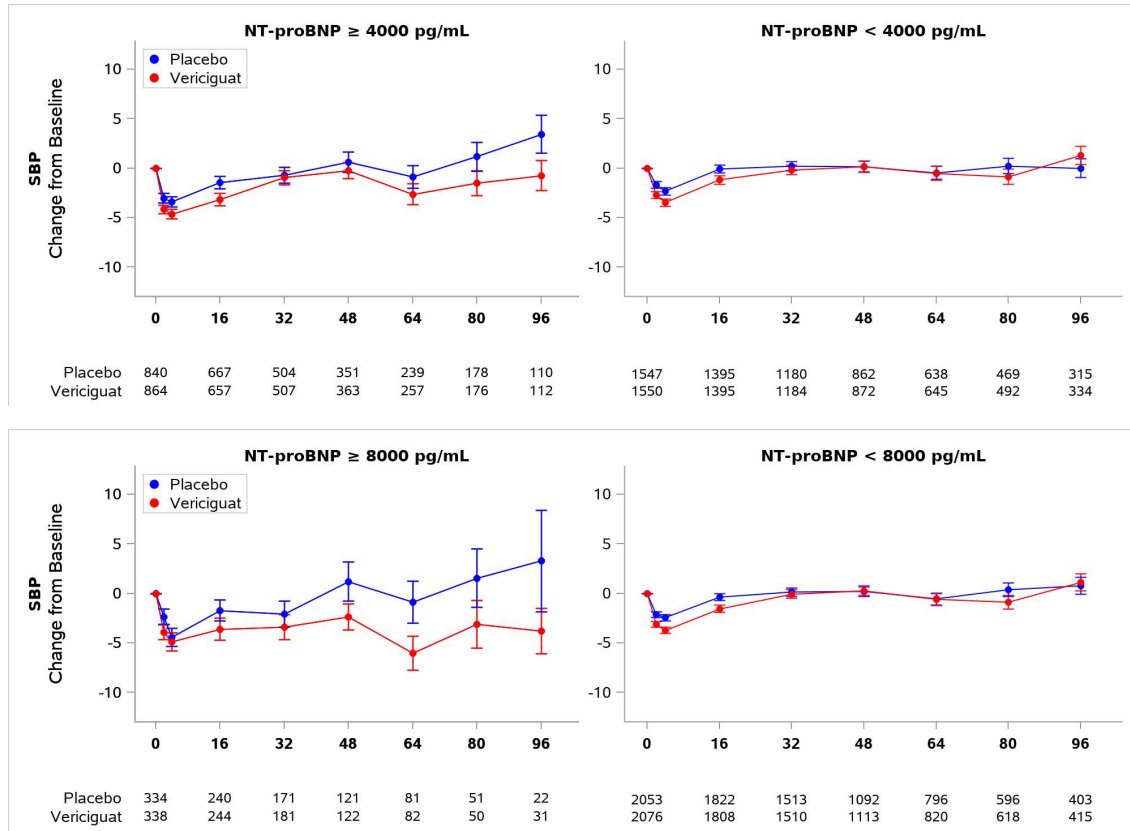


Figure S5. Systolic blood pressure (SBP) trajectory over time in patients time in patients receiving (vs not receiving) SGLT2i

