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	Single dose		Multiple dose		
	Vericiguat n=584 (100%)	Placebo n=167 (100%)	Vericiguat n=175 (100%)	Placebo n=75 (100%)	Total N=692 (100%)
Number (%) of subjects with AEs:					
Any AE	224 (38.4%)	23 (13.8%)	69 (39.4%)	17 (22.7%)	303 (43.8%)
Maximum intensity for any AE					
mild	192 (32.9%)	21 (12.6%)	65 (37.1%)	16 (21.3%)	265 (38.3%)
moderate	32 (5.5%)	2 (1.2%)	4 (2.3%)	1 (1.3%)	38 (5.5%)
Any vericiguat/placebo-related AE	130 (22.3%)	15 (9.0%)	54 (30.9%)	8 (10.7%)	192 (27.7%)
Maximum intensity for any vericiguat/placebo-related AEs					
mild	114 (19.5%)	14 (8.4%)	50 (28.6%)	7 (9.3%)	171 (24.7%)
moderate	16 (2.7%)	1 (0.6%)	4 (2.3%)	1 (1.3%)	21 (3.0%)
Any AE related to procedures required by the protocol	61 (10.4%)	3 (1.8%)	9 (5.1%)	5 (6.7%)	77 (11.1%)
Any AE leading to discontinuation of vericiguat/placebo	4 (0.7%)	2 (1.2%)	1 (0.6%)	0	7 (1.0%)
Any SAE	0	0	0	0	0

Note: vericiguat given as PEG solution, 1.25 mg, 2.5 mg, 5 mg and 10 mg IR tablets, [redacted] mg [redacted] tablet and [redacted] mg [redacted] tablet; vericiguat + interaction drug excluded.

Subjects who received placebo and vericiguat were counted once for each of the treatments and once for total. Subjects who received different vericiguat treatments were counted only once for the pooled treatment. Some subjects have received several treatments in crossover studies.

AE(s): treatment-emergent adverse event(s); SAF: safety analysis set; PEG: polyethylene glycol; [redacted]

Source: 5.3.5.3.1 PH-40726/Table 14.3.1/5, 14.3.1/10, 14.3.1/11

表 2.7.4.8-2 貧血に関連する TEAE の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		243	(9.6)	185	(7.4)	428	(8.5)
with no adverse event		2,276	(90.4)	2,330	(92.6)	4,606	(91.5)
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**235**	**(9.3)**	**174**	**(6.9)**	**409**	**(8.1)**
Anaemia	貧血	192	(7.6)	143	(5.7)	335	(6.7)
Anaemia macrocytic	大球性貧血	1	(0.0)	2	(0.1)	3	(0.1)
Anaemia of chronic disease	慢性疾患の貧血	1	(0.0)	1	(0.0)	2	(0.0)
Autoimmune haemolytic anaemia	自己免疫性溶血性貧血	1	(0.0)	0	(0.0)	1	(0.0)
Blood loss anaemia	失血性貧血	3	(0.1)	2	(0.1)	5	(0.1)
Haemolytic anaemia	溶血性貧血	0	(0.0)	1	(0.0)	1	(0.0)
Hypochromic anaemia	低色素性貧血	2	(0.1)	2	(0.1)	4	(0.1)
Iron deficiency anaemia	鉄欠乏性貧血	27	(1.1)	19	(0.8)	46	(0.9)
Microcytic anaemia	小球性貧血	5	(0.2)	2	(0.1)	7	(0.1)
Nephrogenic anaemia	腎性貧血	1	(0.0)	2	(0.1)	3	(0.1)
Normochromic anaemia	正色素性貧血	0	(0.0)	1	(0.0)	1	(0.0)
Normochromic normocytic anaemia	正色素性正球性貧血	7	(0.3)	3	(0.1)	10	(0.2)
Normocytic anaemia	正球性貧血	2	(0.1)	1	(0.0)	3	(0.1)
Pancytopenia	汎血球減少症	6	(0.2)	1	(0.0)	7	(0.1)
Pernicious anaemia	悪性貧血	0	(0.0)	1	(0.0)	1	(0.0)
Investigations	**臨床検査**	**12**	**(0.5)**	**12**	**(0.5)**	**24**	**(0.5)**
Haematocrit decreased	ヘマトクリット減少	2	(0.1)	2	(0.1)	4	(0.1)
Haemoglobin decreased	ヘモグロビン減少	8	(0.3)	10	(0.4)	18	(0.4)
Red blood cell count decreased	赤血球数減少	4	(0.2)	3	(0.1)	7	(0.1)

Every subject is counted a single time for each applicable row and column.

The Anemia grouping is comprised of the following preferred terms: Anaemia, Anaemia macrocytic, Anaemia of chronic disease, Iron deficiency anaemia, Microcytic anaemia, Autoimmune haemolytic anaemia, Blood loss anaemia, Haemolytic anaemia, Hypochromic anaemia, Nephrogenic anaemia, Normochromic anaemia, Normochromic normocytic anaemia, Normocytic anaemia, Pancytopenia, Pernicious anaemia, Haematocrit decreased, Haemoglobin decreased, and Red blood cell count decreased.

Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.

Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 52

表 2.7.4.8-3 出血関連用語（臨床検査用語を除く）（SMQ）（狭域検索用語）の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		217	(8.6)	256	(10.2)	473	(9.4)
with no adverse event		2,302	(91.4)	2,259	(89.8)	4,561	(90.6)
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**7**	**(0.3)**	**5**	**(0.2)**	**12**	**(0.2)**
Blood loss anaemia	失血性貧血	3	(0.1)	2	(0.1)	5	(0.1)
Disseminated intravascular coagulation	播種性血管内凝固	1	(0.0)	0	(0.0)	1	(0.0)
Haemorrhagic diathesis	出血性素因	0	(0.0)	1	(0.0)	1	(0.0)
Immune thrombocytopenic purpura	免疫性血小板減少性紫斑病	1	(0.0)	0	(0.0)	1	(0.0)
Increased tendency to bruise	内出血発生の増加傾向	1	(0.0)	0	(0.0)	1	(0.0)
Spontaneous haematoma	特発性血腫	1	(0.0)	2	(0.1)	3	(0.1)
Ear and labyrinth disorders	**耳および迷路障害**	**1**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.0)**
Ear haemorrhage	耳出血	1	(0.0)	0	(0.0)	1	(0.0)
Eye disorders	**眼障害**	**12**	**(0.5)**	**16**	**(0.6)**	**28**	**(0.6)**
Conjunctival haemorrhage	結膜出血	5	(0.2)	6	(0.2)	11	(0.2)
Eye haematoma	眼血腫	0	(0.0)	3	(0.1)	3	(0.1)
Eye haemorrhage	眼出血	2	(0.1)	2	(0.1)	4	(0.1)
Retinal haemorrhage	網膜出血	1	(0.0)	1	(0.0)	2	(0.0)
Vitreous haemorrhage	硝子体出血	5	(0.2)	4	(0.2)	9	(0.2)
Gastrointestinal disorders	**胃腸障害**	**63**	**(2.5)**	**64**	**(2.5)**	**127**	**(2.5)**
Abdominal wall haematoma	腹壁血腫	0	(0.0)	1	(0.0)	1	(0.0)
Anal haemorrhage	肛門出血	0	(0.0)	1	(0.0)	1	(0.0)
Gastric haemorrhage	胃出血	4	(0.2)	0	(0.0)	4	(0.1)
Gastric ulcer haemorrhage	出血性胃潰瘍	0	(0.0)	2	(0.1)	2	(0.0)
Gastritis haemorrhagic	出血性胃炎	1	(0.0)	1	(0.0)	2	(0.0)
Gastrointestinal haemorrhage	胃腸出血	14	(0.6)	14	(0.6)	28	(0.6)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Gingival bleeding	歯肉出血	3	(0.1)	3	(0.1)	6	(0.1)
Haematemesis	吐血	3	(0.1)	4	(0.2)	7	(0.1)
Haematochezia	血便排泄	3	(0.1)	8	(0.3)	11	(0.2)
Haemorrhoidal haemorrhage	痔出血	4	(0.2)	4	(0.2)	8	(0.2)
Intestinal haemorrhage	腸出血	0	(0.0)	1	(0.0)	1	(0.0)
Intra-abdominal haematoma	腹腔内血腫	2	(0.1)	1	(0.0)	3	(0.1)
Large intestinal haemorrhage	大腸出血	1	(0.0)	0	(0.0)	1	(0.0)
Large intestinal ulcer haemorrhage	出血性大腸潰瘍	0	(0.0)	1	(0.0)	1	(0.0)
Lower gastrointestinal haemorrhage	下部消化管出血	4	(0.2)	2	(0.1)	6	(0.1)
Melaena	メレナ	4	(0.2)	5	(0.2)	9	(0.2)
Mouth haemorrhage	口腔内出血	3	(0.1)	2	(0.1)	5	(0.1)
Oesophageal varices haemorrhage	食道静脈瘤出血	0	(0.0)	1	(0.0)	1	(0.0)
Oral contusion	口腔挫傷	1	(0.0)	0	(0.0)	1	(0.0)
Peritoneal haemorrhage	腹膜出血	0	(0.0)	1	(0.0)	1	(0.0)
Rectal haemorrhage	直腸出血	14	(0.6)	6	(0.2)	20	(0.4)
Tongue haemorrhage	舌出血	0	(0.0)	1	(0.0)	1	(0.0)
Upper gastrointestinal haemorrhage	上部消化管出血	4	(0.2)	10	(0.4)	14	(0.3)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	7	(0.3)	7	(0.3)	14	(0.3)
Catheter site haematoma	カテーテル留置部位血腫	**0**	**(0.0)**	**1**	**(0.0)**	**1**	**(0.0)**
Catheter site haemorrhage	カテーテル留置部位出血	2	(0.1)	1	(0.0)	3	(0.1)
Haemorrhagic cyst	出血性嚢胞	0	(0.0)	1	(0.0)	1	(0.0)
Implant site haematoma	埋込み部位血腫	2	(0.1)	0	(0.0)	2	(0.0)
Implant site haemorrhage	埋込み部位出血	1	(0.0)	1	(0.0)	2	(0.0)
Medical device site haematoma	医療機器使用部位血腫	2	(0.1)	1	(0.0)	3	(0.1)
Medical device site haemorrhage	医療機器使用部位出血	0	(0.0)	1	(0.0)	1	(0.0)
Vessel puncture site haematoma	血管穿刺部位血腫	0	(0.0)	1	(0.0)	1	(0.0)
Infections and infestations	**感染症および寄生虫症**	**1**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.0)**
Haematoma infection	血腫感染	1	(0.0)	0	(0.0)	1	(0.0)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**45**	**(1.8)**	**53**	**(2.1)**	**98**	**(1.9)**
Bone contusion	骨挫傷	1	(0.0)	0	(0.0)	1	(0.0)
Brain contusion	脳挫傷	0	(0.0)	1	(0.0)	1	(0.0)
Contusion	挫傷	22	(0.9)	33	(1.3)	55	(1.1)
Extradural haematoma	硬膜外血腫	0	(0.0)	1	(0.0)	1	(0.0)
Eye contusion	眼挫傷	2	(0.1)	1	(0.0)	3	(0.1)
Haematuria traumatic	外傷性血尿	0	(0.0)	1	(0.0)	1	(0.0)
Hyphaema	前房出血	1	(0.0)	0	(0.0)	1	(0.0)
Incision site haematoma	切開部位血腫	0	(0.0)	1	(0.0)	1	(0.0)
Incision site haemorrhage	切開部位出血	2	(0.1)	0	(0.0)	2	(0.0)
Muscle contusion	筋挫傷	0	(0.0)	1	(0.0)	1	(0.0)
Periorbital haematoma	眼窩周囲血腫	1	(0.0)	0	(0.0)	1	(0.0)
Post procedural contusion	処置後挫傷	1	(0.0)	0	(0.0)	1	(0.0)
Post procedural haematoma	処置後血腫	0	(0.0)	4	(0.2)	4	(0.1)
Post procedural haematuria	処置後血尿	1	(0.0)	1	(0.0)	2	(0.0)
Post procedural haemorrhage	処置後出血	2	(0.1)	8	(0.3)	10	(0.2)
Pulmonary contusion	肺挫傷	0	(0.0)	1	(0.0)	1	(0.0)
Stoma site haemorrhage	ストーマ部出血	1	(0.0)	0	(0.0)	1	(0.0)
Subcutaneous haematoma	皮下血腫	5	(0.2)	0	(0.0)	5	(0.1)
Subdural haematoma	硬膜下血腫	6	(0.2)	3	(0.1)	9	(0.2)
Subdural haemorrhage	硬膜下出血	0	(0.0)	1	(0.0)	1	(0.0)
Traumatic haematoma	外傷性血腫	2	(0.1)	0	(0.0)	2	(0.0)
Wound haemorrhage	創傷出血	2	(0.1)	1	(0.0)	3	(0.1)
Investigations	**臨床検査**	**1**	**(0.0)**	**1**	**(0.0)**	**2**	**(0.0)**
Blood urine	尿中血	1	(0.0)	0	(0.0)	1	(0.0)
Blood urine present	尿中血陽性	0	(0.0)	1	(0.0)	1	(0.0)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**2**	**(0.1)**	**5**	**(0.2)**	**7**	**(0.1)**
Haemarthrosis	出血性関節症	2	(0.1)	2	(0.1)	4	(0.1)
Haematoma muscle	筋肉内血腫	0	(0.0)	3	(0.1)	3	(0.1)
Nervous system disorders	**神経系障害**	**2**	**(0.1)**	**3**	**(0.1)**	**5**	**(0.1)**
Cerebral haemorrhage	脳出血	1	(0.0)	1	(0.0)	2	(0.0)
Subarachnoid haemorrhage	くも膜下出血	1	(0.0)	1	(0.0)	2	(0.0)
Thalamus haemorrhage	視床出血	0	(0.0)	1	(0.0)	1	(0.0)
Renal and urinary disorders	**腎および尿路障害**	**23**	**(0.9)**	**24**	**(1.0)**	**47**	**(0.9)**
Cystitis haemorrhagic	出血性膀胱炎	1	(0.0)	1	(0.0)	2	(0.0)
Haematuria	血尿	22	(0.9)	23	(0.9)	45	(0.9)
Reproductive system and breast disorders	**生殖系および乳房障害**	**5**	**(0.2)**	**3**	**(0.1)**	**8**	**(0.2)**
Breast haematoma	乳房血腫	0	(0.0)	1	(0.0)	1	(0.0)
Dysfunctional uterine bleeding	機能不全性子宮出血	0	(0.0)	1	(0.0)	1	(0.0)
Haematospermia	血精液症	1	(0.0)	0	(0.0)	1	(0.0)
Menorrhagia	月経過多	0	(0.0)	1	(0.0)	1	(0.0)
Metrorrhagia	不正子宮出血	1	(0.0)	0	(0.0)	1	(0.0)
Postmenopausal haemorrhage	閉経後出血	1	(0.0)	0	(0.0)	1	(0.0)
Vaginal haemorrhage	膣出血	2	(0.1)	0	(0.0)	2	(0.0)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**46**	**(1.8)**	**74**	**(2.9)**	**120**	**(2.4)**
Bronchial haemorrhage	気管支出血	0	(0.0)	1	(0.0)	1	(0.0)
Epistaxis	鼻出血	37	(1.5)	59	(2.3)	96	(1.9)
Haemoptysis	喀血	8	(0.3)	11	(0.4)	19	(0.4)
Haemothorax	血胸	0	(0.0)	3	(0.1)	3	(0.1)
Paranasal sinus haemorrhage	副鼻腔出血	0	(0.0)	1	(0.0)	1	(0.0)
Tonsillar haemorrhage	扁桃出血	1	(0.0)	0	(0.0)	1	(0.0)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**11**	**(0.4)**	**11**	**(0.4)**	**22**	**(0.4)**
Blood blister	血性水疱	0	(0.0)	1	(0.0)	1	(0.0)
Ecchymosis	斑状出血	6	(0.2)	6	(0.2)	12	(0.2)
Haemorrhage subcutaneous	皮下出血	3	(0.1)	2	(0.1)	5	(0.1)
Henoch-Schonlein purpura	ヘノッホ・シェーンライン紫斑病	0	(0.0)	1	(0.0)	1	(0.0)
Petechiae	点状出血	1	(0.0)	0	(0.0)	1	(0.0)
Purpura	紫斑	2	(0.1)	0	(0.0)	2	(0.0)
Vascular purpura	血管性紫斑病	0	(0.0)	1	(0.0)	1	(0.0)
Vascular disorders	**血管障害**	**29**	**(1.2)**	**27**	**(1.1)**	**56**	**(1.1)**
Bleeding varicose vein	出血性静脈瘤	2	(0.1)	3	(0.1)	5	(0.1)
Haematoma	血腫	20	(0.8)	19	(0.8)	39	(0.8)
Haemorrhage	出血	2	(0.1)	1	(0.0)	3	(0.1)
Haemorrhagic vasculitis	出血性血管炎	0	(0.0)	1	(0.0)	1	(0.0)
Internal haemorrhage	内出血	1	(0.0)	0	(0.0)	1	(0.0)
Shock haemorrhagic	出血性ショック	0	(0.0)	2	(0.1)	2	(0.0)
Varicose vein ruptured	静脈瘤破裂	4	(0.2)	1	(0.0)	5	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/ Table 53

表 2.7.4.8-4 急性腎不全（SMQ）（狭域検索用語）の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		278	(11.0)	281	(11.2)	559	(11.1)
with no adverse event		2,241	(89.0)	2,234	(88.8)	4,475	(88.9)
Renal and urinary disorders	**腎および尿路障害**	**278**	**(11.0)**	**281**	**(11.2)**	**559**	**(11.1)**
Acute kidney injury	急性腎障害	134	(5.3)	127	(5.0)	261	(5.2)
Anuria	無尿	1	(0.0)	1	(0.0)	2	(0.0)
Azotaemia	高窒素血症	2	(0.1)	3	(0.1)	5	(0.1)
Nephropathy toxic	中毒性ネフロパシー	0	(0.0)	3	(0.1)	3	(0.1)
Oliguria	乏尿	1	(0.0)	1	(0.0)	2	(0.0)
Prerenal failure	腎前性腎不全	0	(0.0)	1	(0.0)	1	(0.0)
Renal failure	腎不全	92	(3.7)	89	(3.5)	181	(3.6)
Renal impairment	腎機能障害	67	(2.7)	66	(2.6)	133	(2.6)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 54

表 2.7.4.8-5 傷害、転倒及び骨折に関連する TEAE の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		151	(6.0)	167	(6.6)	318	(6.3)
with no adverse event		2,368	(94.0)	2,348	(93.4)	4,716	(93.7)
Gastrointestinal disorders	**胃腸障害**	**1**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.0)**
Oral contusion	口腔挫傷	1	(0.0)	0	(0.0)	1	(0.0)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**150**	**(6.0)**	**165**	**(6.6)**	**315**	**(6.3)**
Acetabulum fracture	寛骨臼骨折	0	(0.0)	1	(0.0)	1	(0.0)
Ankle fracture	足関節部骨折	5	(0.2)	4	(0.2)	9	(0.2)
Back injury	背部損傷	2	(0.1)	1	(0.0)	3	(0.1)
Bone fissure	骨亀裂	1	(0.0)	0	(0.0)	1	(0.0)
Brain contusion	脳挫傷	0	(0.0)	1	(0.0)	1	(0.0)
Cervical vertebral fracture	頚椎骨折	1	(0.0)	0	(0.0)	1	(0.0)
Clavicle fracture	鎖骨骨折	0	(0.0)	3	(0.1)	3	(0.1)
Concussion	脳振盪	3	(0.1)	2	(0.1)	5	(0.1)
Costal cartilage fracture	肋軟骨骨折	0	(0.0)	1	(0.0)	1	(0.0)
Craniocerebral injury	頭蓋脳損傷	2	(0.1)	3	(0.1)	5	(0.1)
Extradural haematoma	硬膜外血腫	0	(0.0)	1	(0.0)	1	(0.0)
Face injury	顔面損傷	1	(0.0)	3	(0.1)	4	(0.1)
Facial bones fracture	顔面骨骨折	3	(0.1)	5	(0.2)	8	(0.2)
Fall	転倒	62	(2.5)	59	(2.3)	121	(2.4)
Femoral neck fracture	大腿骨頚部骨折	2	(0.1)	7	(0.3)	9	(0.2)
Femur fracture	大腿骨骨折	3	(0.1)	12	(0.5)	15	(0.3)
Fibula fracture	腓骨骨折	1	(0.0)	2	(0.1)	3	(0.1)
Foot fracture	足骨折	6	(0.2)	2	(0.1)	8	(0.2)
Forearm fracture	前腕骨折	1	(0.0)	0	(0.0)	1	(0.0)
Fractured coccyx	尾骨骨折	1	(0.0)	0	(0.0)	1	(0.0)
Hand fracture	手骨折	2	(0.1)	2	(0.1)	4	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Head injury	頭部損傷	14	(0.6)	16	(0.6)	30	(0.6)
Hip fracture	股関節部骨折	5	(0.2)	3	(0.1)	8	(0.2)
Humerus fracture	上腕骨骨折	1	(0.0)	7	(0.3)	8	(0.2)
Jaw fracture	顎の骨折	0	(0.0)	1	(0.0)	1	(0.0)
Joint dislocation	関節脱臼	1	(0.0)	2	(0.1)	3	(0.1)
Joint injury	関節損傷	5	(0.2)	6	(0.2)	11	(0.2)
Limb injury	四肢損傷	19	(0.8)	23	(0.9)	42	(0.8)
Lip injury	口唇損傷	1	(0.0)	0	(0.0)	1	(0.0)
Lower limb fracture	下肢骨折	1	(0.0)	3	(0.1)	4	(0.1)
Lumbar vertebral fracture	腰椎骨折	0	(0.0)	2	(0.1)	2	(0.0)
Meniscus injury	半月板損傷	0	(0.0)	1	(0.0)	1	(0.0)
Mouth injury	口腔内損傷	1	(0.0)	0	(0.0)	1	(0.0)
Nasal injury	鼻部損傷	0	(0.0)	1	(0.0)	1	(0.0)
Patella fracture	膝蓋骨骨折	1	(0.0)	0	(0.0)	1	(0.0)
Pelvic fracture	骨盤骨折	0	(0.0)	1	(0.0)	1	(0.0)
Pubis fracture	恥骨骨折	2	(0.1)	1	(0.0)	3	(0.1)
Radius fracture	橈骨骨折	2	(0.1)	1	(0.0)	3	(0.1)
Rib fracture	肋骨骨折	4	(0.2)	11	(0.4)	15	(0.3)
Spinal compression fracture	脊椎圧迫骨折	5	(0.2)	3	(0.1)	8	(0.2)
Spinal fracture	脊椎骨折	2	(0.1)	2	(0.1)	4	(0.1)
Subdural haematoma	硬膜下血腫	6	(0.2)	3	(0.1)	9	(0.2)
Subdural haemorrhage	硬膜下出血	0	(0.0)	1	(0.0)	1	(0.0)
Thoracic vertebral fracture	胸椎骨折	0	(0.0)	1	(0.0)	1	(0.0)
Tibia fracture	脛骨骨折	2	(0.1)	3	(0.1)	5	(0.1)
Tooth fracture	歯牙破折	1	(0.0)	2	(0.1)	3	(0.1)
Traumatic fracture	外傷性骨折	1	(0.0)	0	(0.0)	1	(0.0)
Ulna fracture	尺骨骨折	1	(0.0)	0	(0.0)	1	(0.0)
Upper limb fracture	上肢骨折	2	(0.1)	3	(0.1)	5	(0.1)
Wrist fracture	手首関節骨折	3	(0.1)	1	(0.0)	4	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**0**	**(0.0)**	**2**	**(0.1)**	**2**	**(0.0)**
Pathological fracture	病的骨折	0	(0.0)	2	(0.1)	2	(0.0)

Every subject is counted a single time for each applicable row and column.
The Falls and fractures grouping is comprised of
1. The high group level terms of Bone and joint injuries, Fractures
2. The high level terms of Cerebral injuries NEC, and
3. The preferred terms of Fall, Back injury, Face injury, Head injury, Limb injury, Lip injury, Mouth injury, Nasal injury, Neck injury, Oral contusion, Tooth fracture, and Tooth injury.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 55

表 2.7.4.8-6 症候性低血圧の要約（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

	Vericiguat		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	2519		2515		5034	
with one or more adverse events	229	(9.1)	198	(7.9)	427	(8.5)
by maximum intensity						
mild	102	(4.0)	61	(2.4)	163	(3.2)
moderate	93	(3.7)	95	(3.8)	188	(3.7)
severe	34	(1.3)	42	(1.7)	76	(1.5)
unknown	0	(0.0)	0	(0.0)	0	(0.0)
with an outcome of recovered, recovering, or recovered with sequelae (combined)	223	(8.9)	188	(7.5)	411	(8.2)
with an outcome of not recovered	7	(0.3)	14	(0.6)	21	(0.4)
with an outcome of fatal	0	(0.0)	0	(0.0)	0	(0.0)
with an outcome of unknown	1	(0.0)	0	(0.0)	1	(0.0)
with an action taken of dose reduced	19	(0.8)	16	(0.6)	35	(0.7)
with an action taken of drug interrupted	102	(4.0)	75	(3.0)	177	(3.5)
with an action taken of drug withdrawn	27	(1.1)	20	(0.8)	47	(0.9)
with an action taken of dose not changed	102	(4.0)	103	(4.1)	205	(4.1)
with an action of unknown or not applicable	3	(0.1)	5	(0.2)	8	(0.2)
with drug-related† adverse events	108	(4.3)	92	(3.7)	200	(4.0)
with an action taken of dose reduced	16	(0.6)	14	(0.6)	30	(0.6)
with an action taken of drug interrupted	61	(2.4)	39	(1.6)	100	(2.0)
with an action taken of drug withdrawn	18	(0.7)	14	(0.6)	32	(0.6)
with an action taken of dose not changed	23	(0.9)	36	(1.4)	59	(1.2)
with an action of unknown or not applicable	0	(0.0)	0	(0.0)	0	(0.0)
with serious adverse events	30	(1.2)	37	(1.5)	67	(1.3)
that resulted in significant disability or incapacity	0	(0.0)	0	(0.0)	0	(0.0)
that resulted in hospitalization	27	(1.1)	33	(1.3)	60	(1.2)
that was life threatening	3	(0.1)	3	(0.1)	6	(0.1)
that occurred with an overdose	0	(0.0)	0	(0.0)	0	(0.0)
that resulted in some other medically important event	3	(0.1)	3	(0.1)	6	(0.1)
that resulted in death	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
This table includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
For event intensity, only the most severe intensity across all AEs is counted.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 56

表 2.7.4.8-7 低血圧に関連する TEAE の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		412	(16.4)	375	(14.9)	787	(15.6)
with no adverse event		2,107	(83.6)	2,140	(85.1)	4,247	(84.4)
Investigations	**臨床検査**	**3**	**(0.1)**	**6**	**(0.2)**	**9**	**(0.2)**
Blood pressure decreased	血圧低下	2	(0.1)	5	(0.2)	7	(0.1)
Blood pressure diastolic decreased	拡張期血圧低下	0	(0.0)	1	(0.0)	1	(0.0)
Blood pressure systolic decreased	収縮期血圧低下	1	(0.0)	0	(0.0)	1	(0.0)
Vascular disorders	**血管障害**	**409**	**(16.2)**	**369**	**(14.7)**	**778**	**(15.5)**
Hypotension	低血圧	388	(15.4)	354	(14.1)	742	(14.7)
Orthostatic hypotension	起立性低血圧	33	(1.3)	25	(1.0)	58	(1.2)

Every subject is counted a single time for each applicable row and column.
The Hypotension grouping is comprised of the following preferred terms: Hypotension, Diastolic hypotension, Orthostatic hypotension, Blood pressure decreased, Blood pressure decreased, Blood pressure systolic decreased, Blood pressure diastolic decreased, Blood pressure ambulatory decreased, and Blood pressure systolic inspiratory decreased.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 57

表 2.7.4.8-8 症候性低血圧の 2 日以内に発現した転倒又は骨折（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more symptomatic hypotension adverse events		229	(9.1)	198	(7.9)	427	(8.5)
with one or more symptomatic hypotension adverse events contemporaneous with a fall or fracture†		5	(0.2)	7	(0.3)	12	(0.2)
Falls and Fractures		**5**	**(0.2)**	**7**	**(0.3)**	**12**	**(0.2)**
Back injury	背部損傷	1	(0.0)	0	(0.0)	1	(0.0)
Clavicle fracture	鎖骨骨折	0	(0.0)	1	(0.0)	1	(0.0)
Fall	転倒	3	(0.1)	1	(0.0)	4	(0.1)
Femoral neck fracture	大腿骨頚部骨折	1	(0.0)	0	(0.0)	1	(0.0)
Femur fracture	大腿骨骨折	0	(0.0)	1	(0.0)	1	(0.0)
Head injury	頭部損傷	0	(0.0)	1	(0.0)	1	(0.0)
Joint injury	関節損傷	0	(0.0)	1	(0.0)	1	(0.0)
Limb injury	四肢損傷	1	(0.0)	2	(0.1)	3	(0.1)
Nasal injury	鼻部損傷	0	(0.0)	1	(0.0)	1	(0.0)
Rib fracture	肋骨骨折	0	(0.0)	1	(0.0)	1	(0.0)

Every subject is counted a single time for each applicable row and column.

Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.

† Contemporaneous requires occurrence of the fall or fracture within two days of the event of interest. The Falls and fractures grouping is comprised of 1. The high group level terms of Bone and joint injuries, Fractures 2. The high level terms of Cerebral injuries NEC, and 3. The preferred terms of Fall, Back injury, Face injury, Head injury, Limb injury, Lip injury, Mouth injury, Nasal injury, Neck injury, Oral contusion, Tooth fracture, and Tooth injury.

Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 58

表 2.7.4.8-9 失神の要約（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

	Vericiguat		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	2519		2515		5034	
with one or more adverse events	101	(4.0)	87	(3.5)	188	(3.7)
by maximum intensity						
mild	22	(0.9)	19	(0.8)	41	(0.8)
moderate	34	(1.3)	35	(1.4)	69	(1.4)
severe	45	(1.8)	33	(1.3)	78	(1.5)
unknown	0	(0.0)	0	(0.0)	0	(0.0)
with an outcome of recovered, recovering, or recovered with sequelae (combined)	101	(4.0)	87	(3.5)	188	(3.7)
with an outcome of not recovered	0	(0.0)	0	(0.0)	0	(0.0)
with an outcome of fatal	0	(0.0)	0	(0.0)	0	(0.0)
with an outcome of unknown	0	(0.0)	0	(0.0)	0	(0.0)
with an action taken of dose reduced	0	(0.0)	1	(0.0)	1	(0.0)
with an action taken of drug interrupted	17	(0.7)	12	(0.5)	29	(0.6)
with an action taken of drug withdrawn	1	(0.0)	6	(0.2)	7	(0.1)
with an action taken of dose not changed	78	(3.1)	68	(2.7)	146	(2.9)
with an action of unknown or not applicable	5	(0.2)	4	(0.2)	9	(0.2)
with drug-related† adverse events	7	(0.3)	11	(0.4)	18	(0.4)
with an action taken of dose reduced	0	(0.0)	1	(0.0)	1	(0.0)
with an action taken of drug interrupted	3	(0.1)	3	(0.1)	6	(0.1)
with an action taken of drug withdrawn	0	(0.0)	1	(0.0)	1	(0.0)
with an action taken of dose not changed	4	(0.2)	7	(0.3)	11	(0.2)
with an action of unknown or not applicable	0	(0.0)	0	(0.0)	0	(0.0)
with serious adverse events	43	(1.7)	33	(1.3)	76	(1.5)
that resulted in significant disability or incapacity	1	(0.0)	0	(0.0)	1	(0.0)
that resulted in hospitalization	40	(1.6)	33	(1.3)	73	(1.5)
that was life threatening	9	(0.4)	4	(0.2)	13	(0.3)
that occurred with an overdose	0	(0.0)	0	(0.0)	0	(0.0)
that resulted in some other medically important event	1	(0.0)	0	(0.0)	1	(0.0)
that resulted in death	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
This table includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
For event intensity, only the most severe intensity across all AEs is counted.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 59

表 2.7.4.8-10 失神に関連する TEAE の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		111	(4.4)	95	(3.8)	206	(4.1)
with no adverse event		2,408	(95.6)	2,420	(96.2)	4,828	(95.9)
Nervous system disorders	**神経系障害**	**110**	**(4.4)**	**94**	**(3.7)**	**204**	**(4.1)**
Loss of consciousness	意識消失	2	(0.1)	1	(0.0)	3	(0.1)
Presyncope	失神寸前の状態	11	(0.4)	9	(0.4)	20	(0.4)
Syncope	失神	101	(4.0)	88	(3.5)	189	(3.8)
Vascular disorders	**血管障害**	**2**	**(0.1)**	**1**	**(0.0)**	**3**	**(0.1)**
Circulatory collapse	循環虚脱	2	(0.1)	1	(0.0)	3	(0.1)

Every subject is counted a single time for each applicable row and column.
The Syncope grouping is comprised of the following preferred terms: syncope, presyncope, loss of consciousness, and circulatory collapse.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 60

表 2.7.4.8-11 失神の 2 日以内に発現した転倒又は骨折（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more syncope adverse events		101	(4.0)	87	(3.5)	188	(3.7)
with one or more syncope adverse events contemporaneous with a fall or fracture†		12	(0.5)	14	(0.6)	26	(0.5)
Falls and Fractures		**12**	**(0.5)**	**14**	**(0.6)**	**26**	**(0.5)**
Ankle fracture	足関節部骨折	1	(0.0)	0	(0.0)	1	(0.0)
Clavicle fracture	鎖骨骨折	0	(0.0)	1	(0.0)	1	(0.0)
Concussion	脳振盪	1	(0.0)	2	(0.1)	3	(0.1)
Costal cartilage fracture	肋軟骨骨折	0	(0.0)	1	(0.0)	1	(0.0)
Craniocerebral injury	頭蓋脳損傷	0	(0.0)	1	(0.0)	1	(0.0)
Face injury	顔面損傷	1	(0.0)	1	(0.0)	2	(0.0)
Facial bones fracture	顔面骨骨折	1	(0.0)	1	(0.0)	2	(0.0)
Fall	転倒	3	(0.1)	3	(0.1)	6	(0.1)
Fibula fracture	腓骨骨折	1	(0.0)	0	(0.0)	1	(0.0)
Head injury	頭部損傷	2	(0.1)	6	(0.2)	8	(0.2)
Humerus fracture	上腕骨骨折	0	(0.0)	1	(0.0)	1	(0.0)
Joint injury	関節損傷	2	(0.1)	2	(0.1)	4	(0.1)
Limb injury	四肢損傷	0	(0.0)	1	(0.0)	1	(0.0)
Nasal injury	鼻部損傷	0	(0.0)	1	(0.0)	1	(0.0)
Rib fracture	肋骨骨折	1	(0.0)	1	(0.0)	2	(0.0)
Subdural haematoma	硬膜下血腫	1	(0.0)	0	(0.0)	1	(0.0)

Every subject is counted a single time for each applicable row and column.

Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.

† Contemporaneous requires occurrence of the fall or fracture within two days of the event of interest. The Falls and fractures grouping is comprised of 1. The high group level terms of Bone and joint injuries, Fractures 2. The high level terms of Cerebral injuries NEC, and 3. The preferred terms of Fall, Back injury, Face injury, Head injury, Limb injury, Lip injury, Mouth injury, Nasal injury, Neck injury, Oral contusion, Tooth fracture, and Tooth injury.

Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 61

表 2.7.4.8-12 薬剤に関連する肝障害－重症事象のみ（SMQ）（狭域検索用語）の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		14	(0.6)	14	(0.6)	28	(0.6)
with no adverse event		2,505	(99.4)	2,501	(99.4)	5,006	(99.4)
Gastrointestinal disorders	**胃腸障害**	**4**	**(0.2)**	**5**	**(0.2)**	**9**	**(0.2)**
Ascites	腹水	4	(0.2)	4	(0.2)	8	(0.2)
Oesophageal varices haemorrhage	食道静脈瘤出血	0	(0.0)	1	(0.0)	1	(0.0)
Hepatobiliary disorders	**肝胆道系障害**	**10**	**(0.4)**	**8**	**(0.3)**	**18**	**(0.4)**
Acute hepatic failure	急性肝不全	1	(0.0)	3	(0.1)	4	(0.1)
Hepatic cirrhosis	肝硬変	1	(0.0)	1	(0.0)	2	(0.0)
Hepatic failure	肝不全	1	(0.0)	0	(0.0)	1	(0.0)
Hepatocellular injury	肝細胞損傷	1	(0.0)	0	(0.0)	1	(0.0)
Hepatorenal syndrome	肝腎症候群	0	(0.0)	1	(0.0)	1	(0.0)
Liver disorder	肝障害	1	(0.0)	1	(0.0)	2	(0.0)
Liver injury	肝損傷	5	(0.2)	2	(0.1)	7	(0.1)
Nervous system disorders	**神経系障害**	**0**	**(0.0)**	**1**	**(0.0)**	**1**	**(0.0)**
Hepatic encephalopathy	肝性脳症	0	(0.0)	1	(0.0)	1	(0.0)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 62

表 2.7.4.8-13 TEAE の要約〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q1（1556pg/mL 以下）の被験者、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	599		604		1,203	
with one or more adverse events	485	(81.0)	472	(78.1)	957	(79.6)
with no adverse event	114	(19.0)	132	(21.9)	246	(20.4)
with drug-related† adverse events	97	(16.2)	58	(9.6)	155	(12.9)
with non-serious adverse events	465	(77.6)	457	(75.7)	922	(76.6)
with serious adverse events	186	(31.1)	177	(29.3)	363	(30.2)
with serious drug-related adverse events	7	(1.2)	5	(0.8)	12	(1.0)
with dose modification‡ due to an adverse event	156	(26.0)	113	(18.7)	269	(22.4)
who died§	6	(1.0)	11	(1.8)	17	(1.4)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	36	(6.0)	26	(4.3)	62	(5.2)
discontinued drug due to a drug-related adverse event	16	(2.7)	9	(1.5)	25	(2.1)
discontinued drug due to a serious adverse event	13	(2.2)	12	(2.0)	25	(2.1)
discontinued drug due to a serious drug-related adverse event	4	(0.7)	1	(0.2)	5	(0.4)

† Determined by the investigator to be related to the drug.
‡ Defined as an action taken of dose reduced, drug interrupted or drug withdrawn.
§ Includes adverse events associated with a fatal outcome but does not reflect all deaths reported in the study.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 68

表 2.7.4.8-14 TEAE の要約〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q2（1556pg/mL 超 2816pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	613		588		1,201	
with one or more adverse events	492	(80.3)	475	(80.8)	967	(80.5)
with no adverse event	121	(19.7)	113	(19.2)	234	(19.5)
with drug-related† adverse events	91	(14.8)	75	(12.8)	166	(13.8)
with non-serious adverse events	476	(77.7)	455	(77.4)	931	(77.5)
with serious adverse events	197	(32.1)	190	(32.3)	387	(32.2)
with serious drug-related adverse events	7	(1.1)	5	(0.9)	12	(1.0)
with dose modification‡ due to an adverse event	139	(22.7)	136	(23.1)	275	(22.9)
who died§	14	(2.3)	19	(3.2)	33	(2.7)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	33	(5.4)	33	(5.6)	66	(5.5)
discontinued drug due to a drug-related adverse event	14	(2.3)	13	(2.2)	27	(2.2)
discontinued drug due to a serious adverse event	18	(2.9)	18	(3.1)	36	(3.0)
discontinued drug due to a serious drug-related adverse event	4	(0.7)	2	(0.3)	6	(0.5)

† Determined by the investigator to be related to the drug.
‡ Defined as an action taken of dose reduced, drug interrupted or drug withdrawn.
§ Includes adverse events associated with a fatal outcome but does not reflect all deaths reported in the study.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 69

表 2.7.4.8-15 TEAE の要約〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q3（2816pg/mL 超 5314pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	586		611		1,197	
with one or more adverse events	472	(80.5)	512	(83.8)	984	(82.2)
with no adverse event	114	(19.5)	99	(16.2)	213	(17.8)
with drug-related† adverse events	83	(14.2)	72	(11.8)	155	(12.9)
with non-serious adverse events	450	(76.8)	482	(78.9)	932	(77.9)
with serious adverse events	199	(34.0)	213	(34.9)	412	(34.4)
with serious drug-related adverse events	6	(1.0)	4	(0.7)	10	(0.8)
with dose modification‡ due to an adverse event	169	(28.8)	157	(25.7)	326	(27.2)
who died§	21	(3.6)	14	(2.3)	35	(2.9)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	42	(7.2)	38	(6.2)	80	(6.7)
discontinued drug due to a drug-related adverse event	13	(2.2)	13	(2.1)	26	(2.2)
discontinued drug due to a serious adverse event	21	(3.6)	18	(2.9)	39	(3.3)
discontinued drug due to a serious drug-related adverse event	2	(0.3)	2	(0.3)	4	(0.3)

† Determined by the investigator to be related to the drug.
‡ Defined as an action taken of dose reduced, drug interrupted or drug withdrawn.
§ Includes adverse events associated with a fatal outcome but does not reflect all deaths reported in the study.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 70

表 2.7.4.8-16 TEAE の要約〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q4（5314pg/mL 超）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	616		584		1,200	
with one or more adverse events	491	(79.7)	474	(81.2)	965	(80.4)
with no adverse event	125	(20.3)	110	(18.8)	235	(19.6)
with drug-related† adverse events	74	(12.0)	69	(11.8)	143	(11.9)
with non-serious adverse events	460	(74.7)	438	(75.0)	898	(74.8)
with serious adverse events	211	(34.3)	248	(42.5)	459	(38.3)
with serious drug-related adverse events	8	(1.3)	4	(0.7)	12	(1.0)
with dose modification‡ due to an adverse event	159	(25.8)	163	(27.9)	322	(26.8)
who died§	38	(6.2)	32	(5.5)	70	(5.8)
who died due to a drug-related adverse event	1	(0.2)	0	(0.0)	1	(0.1)
discontinued drug due to an adverse event	49	(8.0)	51	(8.7)	100	(8.3)
discontinued drug due to a drug-related adverse event	17	(2.8)	8	(1.4)	25	(2.1)
discontinued drug due to a serious adverse event	18	(2.9)	34	(5.8)	52	(4.3)
discontinued drug due to a serious drug-related adverse event	3	(0.5)	2	(0.3)	5	(0.4)

† Determined by the investigator to be related to the drug.
‡ Defined as an action taken of dose reduced, drug interrupted or drug withdrawn.
§ Includes adverse events associated with a fatal outcome but does not reflect all deaths reported in the study.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 71

表 2.7.4.8-17 いずれかの群で発現割合が 2%以上の TEAE の器官別大分類〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q1（1556pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		599		604		1,203	
with one or more adverse events		485	(81.0)	472	(78.1)	957	(79.6)
with no adverse events		114	(19.0)	132	(21.9)	246	(20.4)
Blood and lymphatic system disorders	血液およびリンパ系障害	40	(6.7)	37	(6.1)	77	(6.4)
Cardiac disorders	心臓障害	128	(21.4)	136	(22.5)	264	(21.9)
Ear and labyrinth disorders	耳および迷路障害	23	(3.8)	14	(2.3)	37	(3.1)
Endocrine disorders	内分泌障害	18	(3.0)	9	(1.5)	27	(2.2)
Eye disorders	眼障害	35	(5.8)	20	(3.3)	55	(4.6)
Gastrointestinal disorders	胃腸障害	168	(28.0)	127	(21.0)	295	(24.5)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	88	(14.7)	81	(13.4)	169	(14.0)
Hepatobiliary disorders	肝胆道系障害	26	(4.3)	24	(4.0)	50	(4.2)
Infections and infestations	感染症および寄生虫症	193	(32.2)	194	(32.1)	387	(32.2)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	67	(11.2)	64	(10.6)	131	(10.9)
Investigations	臨床検査	56	(9.3)	85	(14.1)	141	(11.7)
Metabolism and nutrition disorders	代謝および栄養障害	110	(18.4)	140	(23.2)	250	(20.8)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	96	(16.0)	80	(13.2)	176	(14.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	22	(3.7)	20	(3.3)	42	(3.5)
Nervous system disorders	神経系障害	126	(21.0)	108	(17.9)	234	(19.5)
Psychiatric disorders	精神障害	27	(4.5)	26	(4.3)	53	(4.4)
Renal and urinary disorders	腎および尿路障害	67	(11.2)	81	(13.4)	148	(12.3)
Reproductive system and breast disorders	生殖系および乳房障害	20	(3.3)	25	(4.1)	45	(3.7)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	102	(17.0)	126	(20.9)	228	(19.0)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	55	(9.2)	52	(8.6)	107	(8.9)
Surgical and medical procedures	外科および内科処置	12	(2.0)	6	(1.0)	18	(1.5)
Vascular disorders	血管障害	128	(21.4)	100	(16.6)	228	(19.0)

Every subject is counted a single time for each applicable row and column.
A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 72

表 2.7.4.8-18 いずれかの群で発現割合が 2%以上の TEAE の器官別大分類〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q2（1556pg/mL 超 2816pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		613		588		1,201	
with one or more adverse events		492	(80.3)	475	(80.8)	967	(80.5)
with no adverse events		121	(19.7)	113	(19.2)	234	(19.5)
Blood and lymphatic system disorders	血液およびリンパ系障害	74	(12.1)	42	(7.1)	116	(9.7)
Cardiac disorders	心臓障害	152	(24.8)	152	(25.9)	304	(25.3)
Ear and labyrinth disorders	耳および迷路障害	15	(2.4)	10	(1.7)	25	(2.1)
Endocrine disorders	内分泌障害	15	(2.4)	12	(2.0)	27	(2.2)
Eye disorders	眼障害	20	(3.3)	25	(4.3)	45	(3.7)
Gastrointestinal disorders	胃腸障害	152	(24.8)	131	(22.3)	283	(23.6)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	99	(16.2)	89	(15.1)	188	(15.7)
Hepatobiliary disorders	肝胆道系障害	31	(5.1)	25	(4.3)	56	(4.7)
Infections and infestations	感染症および寄生虫症	217	(35.4)	221	(37.6)	438	(36.5)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	92	(15.0)	67	(11.4)	159	(13.2)
Investigations	臨床検査	86	(14.0)	89	(15.1)	175	(14.6)
Metabolism and nutrition disorders	代謝および栄養障害	142	(23.2)	135	(23.0)	277	(23.1)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	79	(12.9)	88	(15.0)	167	(13.9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	23	(3.8)	22	(3.7)	45	(3.7)
Nervous system disorders	神経系障害	116	(18.9)	96	(16.3)	212	(17.7)
Psychiatric disorders	精神障害	27	(4.4)	35	(6.0)	62	(5.2)
Renal and urinary disorders	腎および尿路障害	95	(15.5)	93	(15.8)	188	(15.7)
Reproductive system and breast disorders	生殖系および乳房障害	28	(4.6)	21	(3.6)	49	(4.1)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	108	(17.6)	115	(19.6)	223	(18.6)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	52	(8.5)	62	(10.5)	114	(9.5)
Surgical and medical procedures	外科および内科処置	12	(2.0)	15	(2.6)	27	(2.2)
Vascular disorders	血管障害	141	(23.0)	112	(19.0)	253	(21.1)

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A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 73

表 2.7.4.8-19 いずれかの群で発現割合が 2%以上の TEAE の器官別大分類〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q3（2816pg/mL 超 5314pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		586		611		1,197	
with one or more adverse events		472	(80.5)	512	(83.8)	984	(82.2)
with no adverse events		114	(19.5)	99	(16.2)	213	(17.8)
Blood and lymphatic system disorders	血液およびリンパ系障害	70	(11.9)	59	(9.7)	129	(10.8)
Cardiac disorders	心臓障害	143	(24.4)	170	(27.8)	313	(26.1)
Ear and labyrinth disorders	耳および迷路障害	17	(2.9)	16	(2.6)	33	(2.8)
Endocrine disorders	内分泌障害	13	(2.2)	17	(2.8)	30	(2.5)
Eye disorders	眼障害	17	(2.9)	30	(4.9)	47	(3.9)
Gastrointestinal disorders	胃腸障害	145	(24.7)	129	(21.1)	274	(22.9)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	75	(12.8)	99	(16.2)	174	(14.5)
Hepatobiliary disorders	肝胆道系障害	29	(4.9)	33	(5.4)	62	(5.2)
Infections and infestations	感染症および寄生虫症	224	(38.2)	223	(36.5)	447	(37.3)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	72	(12.3)	71	(11.6)	143	(11.9)
Investigations	臨床検査	91	(15.5)	99	(16.2)	190	(15.9)
Metabolism and nutrition disorders	代謝および栄養障害	123	(21.0)	153	(25.0)	276	(23.1)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	65	(11.1)	105	(17.2)	170	(14.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	22	(3.8)	11	(1.8)	33	(2.8)
Nervous system disorders	神経系障害	110	(18.8)	112	(18.3)	222	(18.5)
Psychiatric disorders	精神障害	28	(4.8)	32	(5.2)	60	(5.0)
Renal and urinary disorders	腎および尿路障害	114	(19.5)	111	(18.2)	225	(18.8)
Reproductive system and breast disorders	生殖系および乳房障害	14	(2.4)	30	(4.9)	44	(3.7)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	127	(21.7)	134	(21.9)	261	(21.8)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	51	(8.7)	47	(7.7)	98	(8.2)
Surgical and medical procedures	外科および内科処置	5	(0.9)	13	(2.1)	18	(1.5)
Vascular disorders	血管障害	136	(23.2)	143	(23.4)	279	(23.3)

Every subject is counted a single time for each applicable row and column.
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Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 74

表 2.7.4.8-20 いずれかの群で発現割合が 2%以上の TEAE の器官別大分類〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q4（5314pg/mL 超）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		616		584		1,200	
with one or more adverse events		491	(79.7)	474	(81.2)	965	(80.4)
with no adverse events		125	(20.3)	110	(18.8)	235	(19.6)
Blood and lymphatic system disorders	血液およびリンパ系障害	69	(11.2)	65	(11.1)	134	(11.2)
Cardiac disorders	心臓障害	135	(21.9)	155	(26.5)	290	(24.2)
Endocrine disorders	内分泌障害	13	(2.1)	12	(2.1)	25	(2.1)
Eye disorders	眼障害	16	(2.6)	27	(4.6)	43	(3.6)
Gastrointestinal disorders	胃腸障害	141	(22.9)	134	(22.9)	275	(22.9)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	91	(14.8)	98	(16.8)	189	(15.8)
Hepatobiliary disorders	肝胆道系障害	32	(5.2)	32	(5.5)	64	(5.3)
Infections and infestations	感染症および寄生虫症	206	(33.4)	200	(34.2)	406	(33.8)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	69	(11.2)	97	(16.6)	166	(13.8)
Investigations	臨床検査	113	(18.3)	93	(15.9)	206	(17.2)
Metabolism and nutrition disorders	代謝および栄養障害	150	(24.4)	151	(25.9)	301	(25.1)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	67	(10.9)	65	(11.1)	132	(11.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	13	(2.1)	18	(3.1)	31	(2.6)
Nervous system disorders	神経系障害	90	(14.6)	101	(17.3)	191	(15.9)
Psychiatric disorders	精神障害	23	(3.7)	37	(6.3)	60	(5.0)
Renal and urinary disorders	腎および尿路障害	136	(22.1)	133	(22.8)	269	(22.4)
Reproductive system and breast disorders	生殖系および乳房障害	16	(2.6)	16	(2.7)	32	(2.7)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	130	(21.1)	108	(18.5)	238	(19.8)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	55	(8.9)	54	(9.2)	109	(9.1)
Vascular disorders	血管障害	123	(20.0)	123	(21.1)	246	(20.5)

Every subject is counted a single time for each applicable row and column.
A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 75

表 2.7.4.8-21 いずれかの群で発現割合が 2%以上の重篤な TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q1（1556pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		599		604		1,203	
with one or more serious adverse events		186	(31.1)	177	(29.3)	363	(30.2)
with no serious adverse events		413	(68.9)	427	(70.7)	840	(69.8)
Cardiac disorders	**心臓障害**	**41**	**(6.8)**	**56**	**(9.3)**	**97**	**(8.1)**
Cardiac failure	心不全	15	(2.5)	23	(3.8)	38	(3.2)
Gastrointestinal disorders	**胃腸障害**	**22**	**(3.7)**	**16**	**(2.6)**	**38**	**(3.2)**
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**14**	**(2.3)**	**8**	**(1.3)**	**22**	**(1.8)**
Infections and infestations	**感染症および寄生虫症**	**54**	**(9.0)**	**46**	**(7.6)**	**100**	**(8.3)**
Pneumonia	肺炎	23	(3.8)	17	(2.8)	40	(3.3)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**15**	**(2.5)**	**14**	**(2.3)**	**29**	**(2.4)**
Metabolism and nutrition disorders	**代謝および栄養障害**	**14**	**(2.3)**	**15**	**(2.5)**	**29**	**(2.4)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）**	**13**	**(2.2)**	**12**	**(2.0)**	**25**	**(2.1)**
Nervous system disorders	**神経系障害**	**21**	**(3.5)**	**23**	**(3.8)**	**44**	**(3.7)**
Syncope	失神	9	(1.5)	12	(2.0)	21	(1.7)
Renal and urinary disorders	**腎および尿路障害**	**12**	**(2.0)**	**21**	**(3.5)**	**33**	**(2.7)**
Acute kidney injury	急性腎障害	5	(0.8)	13	(2.2)	18	(1.5)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**22**	**(3.7)**	**20**	**(3.3)**	**42**	**(3.5)**
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	12	(2.0)	7	(1.2)	19	(1.6)
Vascular disorders	**血管障害**	**20**	**(3.3)**	**16**	**(2.6)**	**36**	**(3.0)**

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 76

表 2.7.4.8-22 いずれかの群で発現割合が 2%以上の重篤な TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q2（1556pg/mL 超 2816pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		613		588		1,201	
with one or more serious adverse events		197	(32.1)	190	(32.3)	387	(32.2)
with no serious adverse events		416	(67.9)	398	(67.7)	814	(67.8)
Blood and lymphatic system disorders	血液およびリンパ系障害	**12**	**(2.0)**	**6**	**(1.0)**	**18**	**(1.5)**
Cardiac disorders	心臓障害	**47**	**(7.7)**	**61**	**(10.4)**	**108**	**(9.0)**
Cardiac failure	心不全	21	(3.4)	28	(4.8)	49	(4.1)
Gastrointestinal disorders	胃腸障害	**18**	**(2.9)**	**31**	**(5.3)**	**49**	**(4.1)**
Infections and infestations	感染症および寄生虫症	**72**	**(11.7)**	**61**	**(10.4)**	**133**	**(11.1)**
Pneumonia	肺炎	22	(3.6)	26	(4.4)	48	(4.0)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	**14**	**(2.3)**	**15**	**(2.6)**	**29**	**(2.4)**
Metabolism and nutrition disorders	代謝および栄養障害	**19**	**(3.1)**	**29**	**(4.9)**	**48**	**(4.0)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	**16**	**(2.6)**	**15**	**(2.6)**	**31**	**(2.6)**
Nervous system disorders	神経系障害	**18**	**(2.9)**	**13**	**(2.2)**	**31**	**(2.6)**
Syncope	失神	12	(2.0)	3	(0.5)	15	(1.2)
Renal and urinary disorders	腎および尿路障害	**31**	**(5.1)**	**27**	**(4.6)**	**58**	**(4.8)**
Acute kidney injury	急性腎障害	18	(2.9)	16	(2.7)	34	(2.8)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	**14**	**(2.3)**	**21**	**(3.6)**	**35**	**(2.9)**
Vascular disorders	血管障害	**23**	**(3.8)**	**21**	**(3.6)**	**44**	**(3.7)**

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 77

表 2.7.4.8-23 いずれかの群で発現割合が 2%以上の重篤な TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q3（2816pg/mL 超 5314pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		586		611		1,197	
with one or more serious adverse events		199	(34.0)	213	(34.9)	412	(34.4)
with no serious adverse events		387	(66.0)	398	(65.1)	785	(65.6)
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**13**	**(2.2)**	**12**	**(2.0)**	**25**	**(2.1)**
Cardiac disorders	**心臓障害**	**54**	**(9.2)**	**65**	**(10.6)**	**119**	**(9.9)**
Cardiac failure	心不全	24	(4.1)	25	(4.1)	49	(4.1)
Gastrointestinal disorders	**胃腸障害**	**26**	**(4.4)**	**14**	**(2.3)**	**40**	**(3.3)**
Infections and infestations	**感染症および寄生虫症**	**59**	**(10.1)**	**76**	**(12.4)**	**135**	**(11.3)**
Pneumonia	肺炎	19	(3.2)	27	(4.4)	46	(3.8)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**20**	**(3.4)**	**17**	**(2.8)**	**37**	**(3.1)**
Metabolism and nutrition disorders	**代謝および栄養障害**	**20**	**(3.4)**	**15**	**(2.5)**	**35**	**(2.9)**
Nervous system disorders	**神経系障害**	**22**	**(3.8)**	**16**	**(2.6)**	**38**	**(3.2)**
Syncope	失神	12	(2.0)	6	(1.0)	18	(1.5)
Renal and urinary disorders	**腎および尿路障害**	**38**	**(6.5)**	**33**	**(5.4)**	**71**	**(5.9)**
Acute kidney injury	急性腎障害	13	(2.2)	6	(1.0)	19	(1.6)
Chronic kidney disease	慢性腎臓病	11	(1.9)	12	(2.0)	23	(1.9)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**25**	**(4.3)**	**23**	**(3.8)**	**48**	**(4.0)**
Vascular disorders	**血管障害**	**23**	**(3.9)**	**25**	**(4.1)**	**48**	**(4.0)**
Hypotension	低血圧	11	(1.9)	12	(2.0)	23	(1.9)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 78

表 2.7.4.8-24 いずれかの群で発現割合が 2%以上の重篤な TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q4（5314pg/mL 超）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		616		584		1,200	
with one or more serious adverse events		211	(34.3)	248	(42.5)	459	(38.3)
with no serious adverse events		405	(65.7)	336	(57.5)	741	(61.8)
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**16**	**(2.6)**	**8**	**(1.4)**	**24**	**(2.0)**
Anaemia	貧血	13	(2.1)	4	(0.7)	17	(1.4)
Cardiac disorders	**心臓障害**	**51**	**(8.3)**	**71**	**(12.2)**	**122**	**(10.2)**
Cardiac failure	心不全	19	(3.1)	28	(4.8)	47	(3.9)
Gastrointestinal disorders	**胃腸障害**	**25**	**(4.1)**	**27**	**(4.6)**	**52**	**(4.3)**
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**5**	**(0.8)**	**16**	**(2.7)**	**21**	**(1.8)**
Hepatobiliary disorders	**肝胆道系障害**	**13**	**(2.1)**	**5**	**(0.9)**	**18**	**(1.5)**
Infections and infestations	**感染症および寄生虫症**	**73**	**(11.9)**	**71**	**(12.2)**	**144**	**(12.0)**
Pneumonia	肺炎	30	(4.9)	34	(5.8)	64	(5.3)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**13**	**(2.1)**	**24**	**(4.1)**	**37**	**(3.1)**
Metabolism and nutrition disorders	**代謝および栄養障害**	**19**	**(3.1)**	**26**	**(4.5)**	**45**	**(3.8)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）**	**10**	**(1.6)**	**12**	**(2.1)**	**22**	**(1.8)**
Nervous system disorders	**神経系障害**	**17**	**(2.8)**	**24**	**(4.1)**	**41**	**(3.4)**
Renal and urinary disorders	**腎および尿路障害**	**57**	**(9.3)**	**49**	**(8.4)**	**106**	**(8.8)**
Acute kidney injury	急性腎障害	27	(4.4)	14	(2.4)	41	(3.4)
Chronic kidney disease	慢性腎臓病	15	(2.4)	13	(2.2)	28	(2.3)
Renal failure	腎不全	9	(1.5)	14	(2.4)	23	(1.9)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**21**	**(3.4)**	**22**	**(3.8)**	**43**	**(3.6)**

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Vascular disorders	**血管障害**	**13**	**(2.1)**	**18**	**(3.1)**	**31**	**(2.6)**
Hypotension	低血圧	6	(1.0)	13	(2.2)	19	(1.6)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 79

表 2.7.4.8-25 投与中止に至った TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q1（1556pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		599		604		1,203	
with one or more adverse events leading to treatment discontinuation		36	(6.0)	26	(4.3)	62	(5.2)
with no adverse events leading to treatment discontinuation		563	(94.0)	578	(95.7)	1,141	(94.8)
Cardiac disorders	**心臓障害**	**3**	**(0.5)**	**1**	**(0.2)**	**4**	**(0.3)**
Cardiac arrest	心停止	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac failure	心不全	1	(0.2)	1	(0.2)	2	(0.2)
Ventricular tachycardia	心室性頻脈	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**耳および迷路障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Vertigo	回転性めまい	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**眼障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Diplopia	複視	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**胃腸障害**	**6**	**(1.0)**	**3**	**(0.5)**	**9**	**(0.7)**
Abdominal distension	腹部膨満	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	腹痛	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	下痢	0	(0.0)	1	(0.2)	1	(0.1)
Dyspepsia	消化不良	2	(0.3)	0	(0.0)	2	(0.2)
Gastritis	胃炎	0	(0.0)	1	(0.2)	1	(0.1)
Gastrointestinal angiodysplasia	胃腸管血管異形成	0	(0.0)	1	(0.2)	1	(0.1)
Gastrooesophageal reflux disease	胃食道逆流性疾患	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	悪心	1	(0.2)	0	(0.0)	1	(0.1)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**
Asthenia	無力症	2	(0.3)	1	(0.2)	3	(0.2)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Hepatobiliary disorders	**肝胆道系障害**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Hepatic function abnormal	肝機能異常	0	(0.0)	1	(0.2)	1	(0.1)
Immune system disorders	**免疫系障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Seasonal allergy	季節性アレルギー	1	(0.2)	0	(0.0)	1	(0.1)
Infections and infestations	**感染症および寄生虫症**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Cellulitis	蜂巣炎	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonia	肺炎	1	(0.2)	0	(0.0)	1	(0.1)
Investigations	**臨床検査**	**5**	**(0.8)**	**2**	**(0.3)**	**7**	**(0.6)**
Blood creatinine increased	血中クレアチニン増加	2	(0.3)	1	(0.2)	3	(0.2)
Cardiac index abnormal	心指数異常	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1	(0.2)	1	(0.2)	2	(0.2)
Hepatic enzyme increased	肝酵素上昇	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**代謝および栄養障害**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.2)**
Appetite disorder	食欲障害	1	(0.2)	0	(0.0)	1	(0.1)
Gout	痛風	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Myalgia	筋肉痛	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Pancreatic carcinoma	膵癌	0	(0.0)	1	(0.2)	1	(0.1)
Nervous system disorders	**神経系障害**	**6**	**(1.0)**	**1**	**(0.2)**	**7**	**(0.6)**
Axonal neuropathy	軸索型ニューロパチー	1	(0.2)	0	(0.0)	1	(0.1)
Brain injury	脳損傷	1	(0.2)	0	(0.0)	1	(0.1)
Dizziness	浮動性めまい	3	(0.5)	1	(0.2)	4	(0.3)
Dysgeusia	味覚異常	1	(0.2)	0	(0.0)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Psychiatric disorders	**精神障害**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Sleep disorder	睡眠障害	0	(0.0)	1	(0.2)	1	(0.1)
Renal and urinary disorders	**腎および尿路障害**	**4**	**(0.7)**	**7**	**(1.2)**	**11**	**(0.9)**
Acute kidney injury	急性腎障害	3	(0.5)	4	(0.7)	7	(0.6)
Chronic kidney disease	慢性腎臓病	0	(0.0)	2	(0.3)	2	(0.2)
Haematuria	血尿	1	(0.2)	0	(0.0)	1	(0.1)
Renal failure	腎不全	0	(0.0)	1	(0.2)	1	(0.1)
Reproductive system and breast disorders	**生殖系および乳房障害**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Erectile dysfunction	勃起不全	0	(0.0)	1	(0.2)	1	(0.1)
Erection increased	勃起増強	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.2)**
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1	(0.2)	0	(0.0)	1	(0.1)
Interstitial lung disease	間質性肺疾患	0	(0.0)	1	(0.2)	1	(0.1)
Nasal congestion	鼻閉	0	(0.0)	1	(0.2)	1	(0.1)
Productive cough	湿性咳嗽	0	(0.0)	1	(0.2)	1	(0.1)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**2**	**(0.3)**	**3**	**(0.5)**	**5**	**(0.4)**
Henoch-Schonlein purpura	ヘノッホ・シェーンライン紫斑病	0	(0.0)	1	(0.2)	1	(0.1)
Pruritus	そう痒症	0	(0.0)	1	(0.2)	1	(0.1)
Psoriasis	乾癬	1	(0.2)	0	(0.0)	1	(0.1)
Rash	発疹	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	蕁麻疹	0	(0.0)	1	(0.2)	1	(0.1)
Vascular disorders	**血管障害**	**8**	**(1.3)**	**5**	**(0.8)**	**13**	**(1.1)**
Hypotension	低血圧	8	(1.3)	5	(0.8)	13	(1.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 80

表 2.7.4.8-26 投与中止に至った TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q2（1556pg/mL 超 2816pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		613		588		1,201	
with one or more adverse events leading to treatment discontinuation		33	(5.4)	33	(5.6)	66	(5.5)
with no adverse events leading to treatment discontinuation		580	(94.6)	555	(94.4)	1,135	(94.5)
Cardiac disorders	**心臓障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Cardiac failure	心不全	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**耳および迷路障害**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Vertigo	回転性めまい	1	(0.2)	1	(0.2)	2	(0.2)
Gastrointestinal disorders	**胃腸障害**	**2**	**(0.3)**	**7**	**(1.2)**	**9**	**(0.7)**
Constipation	便秘	0	(0.0)	1	(0.2)	1	(0.1)
Diarrhoea	下痢	0	(0.0)	1	(0.2)	1	(0.1)
Dyspepsia	消化不良	0	(0.0)	1	(0.2)	1	(0.1)
Gastritis	胃炎	0	(0.0)	1	(0.2)	1	(0.1)
Gastrointestinal haemorrhage	胃腸出血	0	(0.0)	1	(0.2)	1	(0.1)
Nausea	悪心	1	(0.2)	1	(0.2)	2	(0.2)
Oesophageal varices haemorrhage	食道静脈瘤出血	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatolithiasis	膵石症	1	(0.2)	0	(0.0)	1	(0.1)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.2)**
Asthenia	無力症	1	(0.2)	0	(0.0)	1	(0.1)
General physical health deterioration	全身健康状態悪化	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**肝胆道系障害**	**3**	**(0.5)**	**0**	**(0.0)**	**3**	**(0.2)**
Hepatic congestion	肝臓うっ血	1	(0.2)	0	(0.0)	1	(0.1)
Liver disorder	肝障害	1	(0.2)	0	(0.0)	1	(0.1)
Liver injury	肝損傷	1	(0.2)	0	(0.0)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Infections and infestations	**感染症および寄生虫症**	**0**	**(0.0)**	**6**	**(1.0)**	**6**	**(0.5)**
Device related infection	医療機器関連感染	0	(0.0)	1	(0.2)	1	(0.1)
Gastroenteritis	胃腸炎	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonia	肺炎	0	(0.0)	3	(0.5)	3	(0.2)
Pneumonia bacterial	細菌性肺炎	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**
Asbestosis	石綿肺症	1	(0.2)	0	(0.0)	1	(0.1)
Femoral neck fracture	大腿骨頚部骨折	0	(0.0)	1	(0.2)	1	(0.1)
Intentional overdose	企図的過量投与	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**代謝および栄養障害**	**0**	**(0.0)**	**2**	**(0.3)**	**2**	**(0.2)**
Hypercalcaemia	高カルシウム血症	0	(0.0)	1	(0.2)	1	(0.1)
Hyperkalaemia	高カリウム血症	0	(0.0)	1	(0.2)	1	(0.1)
Ketoacidosis	ケトアシドーシス	0	(0.0)	1	(0.2)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）**	**4**	**(0.7)**	**3**	**(0.5)**	**7**	**(0.6)**
Breast cancer	乳癌	0	(0.0)	1	(0.2)	1	(0.1)
Bronchial carcinoma	気管支癌	1	(0.2)	0	(0.0)	1	(0.1)
Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	0	(0.0)	1	(0.2)	1	(0.1)
Hepatic cancer metastatic	遠隔転移を伴う肝癌	0	(0.0)	1	(0.2)	1	(0.1)
Lung cancer metastatic	遠隔転移を伴う肺癌	1	(0.2)	0	(0.0)	1	(0.1)
Oesophageal carcinoma	食道癌	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatic carcinoma metastatic	遠隔転移を伴う膵癌	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**神経系障害**	**1**	**(0.2)**	**3**	**(0.5)**	**4**	**(0.3)**
Cognitive disorder	認知障害	0	(0.0)	1	(0.2)	1	(0.1)
Somnolence	傾眠	0	(0.0)	1	(0.2)	1	(0.1)
Syncope	失神	1	(0.2)	1	(0.2)	2	(0.2)
Psychiatric disorders	**精神障害**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Restlessness	落ち着きのなさ	0	(0.0)	1	(0.2)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Suicide attempt	自殺企図	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**腎および尿路障害**	**5**	**(0.8)**	**4**	**(0.7)**	**9**	**(0.7)**
Acute kidney injury	急性腎障害	2	(0.3)	2	(0.3)	4	(0.3)
Chronic kidney disease	慢性腎臓病	3	(0.5)	1	(0.2)	4	(0.3)
Renal cyst	腎嚢胞	0	(0.0)	1	(0.2)	1	(0.1)
Reproductive system and breast disorders	**生殖系および乳房障害**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Gynaecomastia	女性化乳房	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.2)**
Acute respiratory failure	急性呼吸不全	0	(0.0)	1	(0.2)	1	(0.1)
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	0	(0.0)	1	(0.2)	1	(0.1)
Dyspnoea	呼吸困難	1	(0.2)	0	(0.0)	1	(0.1)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Dermatitis bullous	水疱性皮膚炎	0	(0.0)	1	(0.2)	1	(0.1)
Surgical and medical procedures	**外科および内科処置**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Cardioversion	心臓除細動	1	(0.2)	0	(0.0)	1	(0.1)
Vascular disorders	**血管障害**	**13**	**(2.1)**	**10**	**(1.7)**	**23**	**(1.9)**
Hypertension	高血圧	0	(0.0)	1	(0.2)	1	(0.1)
Hypotension	低血圧	13	(2.1)	9	(1.5)	22	(1.8)

Every subject is counted a single time for each applicable row and column.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 81

表 2.7.4.8-27 投与中止に至った TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q3（2816pg/mL 超 5314pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		586		611		1,197	
with one or more adverse events leading to treatment discontinuation		42	(7.2)	38	(6.2)	80	(6.7)
with no adverse events leading to treatment discontinuation		544	(92.8)	573	(93.8)	1,117	(93.3)
Cardiac disorders	**心臓障害**	**2**	**(0.3)**	**5**	**(0.8)**	**7**	**(0.6)**
Angina pectoris	狭心症	1	(0.2)	0	(0.0)	1	(0.1)
Aortic valve calcification	大動脈弁石灰化	1	(0.2)	0	(0.0)	1	(0.1)
Aortic valve stenosis	大動脈弁狭窄	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure	心不全	0	(0.0)	2	(0.3)	2	(0.2)
Cardiac failure chronic	慢性心不全	0	(0.0)	1	(0.2)	1	(0.1)
Cardio-respiratory arrest	心肺停止	0	(0.0)	1	(0.2)	1	(0.1)
Ear and labyrinth disorders	**耳および迷路障害**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Vertigo	回転性めまい	0	(0.0)	1	(0.2)	1	(0.1)
Endocrine disorders	**内分泌障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Carcinoid syndrome	カルチノイド症候群	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**胃腸障害**	**6**	**(1.0)**	**1**	**(0.2)**	**7**	**(0.6)**
Abdominal discomfort	腹部不快感	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	腹痛	0	(0.0)	1	(0.2)	1	(0.1)
Ascites	腹水	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	下痢	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	消化不良	1	(0.2)	0	(0.0)	1	(0.1)
Faeces discoloured	変色便	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	悪心	3	(0.5)	0	(0.0)	3	(0.3)
Vomiting	嘔吐	1	(0.2)	0	(0.0)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**2**	**(0.3)**	**2**	**(0.3)**	**4**	**(0.3)**
Chest discomfort	胸部不快感	0	(0.0)	1	(0.2)	1	(0.1)
Chest pain	胸痛	1	(0.2)	1	(0.2)	2	(0.2)
General physical health deterioration	全身健康状態悪化	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**肝胆道系障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Ischaemic hepatitis	虚血性肝炎	1	(0.2)	0	(0.0)	1	(0.1)
Immune system disorders	**免疫系障害**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.2)**
Hypersensitivity	過敏症	2	(0.3)	0	(0.0)	2	(0.2)
Infections and infestations	**感染症および寄生虫症**	**3**	**(0.5)**	**2**	**(0.3)**	**5**	**(0.4)**
Intervertebral discitis	椎間板炎	1	(0.2)	0	(0.0)	1	(0.1)
Necrotising fasciitis	壊死性筋膜炎	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	肺炎	1	(0.2)	0	(0.0)	1	(0.1)
Septic shock	敗血症性ショック	0	(0.0)	1	(0.2)	1	(0.1)
Upper respiratory tract infection	上気道感染	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.3)**
Cervical vertebral fracture	頚椎骨折	1	(0.2)	0	(0.0)	1	(0.1)
Femoral neck fracture	大腿骨頚部骨折	0	(0.0)	1	(0.2)	1	(0.1)
Limb injury	四肢損傷	1	(0.2)	0	(0.0)	1	(0.1)
Investigations	**臨床検査**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.3)**
Hepatic enzyme increased	肝酵素上昇	1	(0.2)	0	(0.0)	1	(0.1)
Platelet count decreased	血小板数減少	1	(0.2)	0	(0.0)	1	(0.1)
Weight increased	体重増加	0	(0.0)	1	(0.2)	1	(0.1)
Metabolism and nutrition disorders	**代謝および栄養障害**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.3)**
Hyperkalaemia	高カリウム血症	0	(0.0)	1	(0.2)	1	(0.1)
Marasmus	マラスムス	1	(0.2)	0	(0.0)	1	(0.1)
Metabolic acidosis	代謝性アシドーシス	0	(0.0)	1	(0.2)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Haematoma muscle	筋肉内血腫	0	(0.0)	1	(0.2)	1	(0.1)
Sjogren's syndrome	シェーグレン症候群	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Lung neoplasm malignant	肺の悪性新生物	0	(0.0)	1	(0.2)	1	(0.1)
Nervous system disorders	**神経系障害**	**6**	**(1.0)**	**5**	**(0.8)**	**11**	**(0.9)**
Brain injury	脳損傷	1	(0.2)	0	(0.0)	1	(0.1)
Dementia	認知症	1	(0.2)	0	(0.0)	1	(0.1)
Dizziness	浮動性めまい	3	(0.5)	1	(0.2)	4	(0.3)
Dyskinesia	ジスキネジア	0	(0.0)	1	(0.2)	1	(0.1)
Hypoxic-ischaemic encephalopathy	低酸素性虚血性脳症	1	(0.2)	1	(0.2)	2	(0.2)
Syncope	失神	0	(0.0)	2	(0.3)	2	(0.2)
Psychiatric disorders	**精神障害**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Depressed mood	抑うつ気分	0	(0.0)	1	(0.2)	1	(0.1)
Drug use disorder	薬物使用障害	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**腎および尿路障害**	**4**	**(0.7)**	**10**	**(1.6)**	**14**	**(1.2)**
Acute kidney injury	急性腎障害	1	(0.2)	2	(0.3)	3	(0.3)
Chronic kidney disease	慢性腎臓病	2	(0.3)	3	(0.5)	5	(0.4)
Renal failure	腎不全	1	(0.2)	4	(0.7)	5	(0.4)
Renal impairment	腎機能障害	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**3**	**(0.5)**	**1**	**(0.2)**	**4**	**(0.3)**
Acute respiratory failure	急性呼吸不全	1	(0.2)	0	(0.0)	1	(0.1)
Haemoptysis	喀血	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary hypertension	肺高血圧症	1	(0.2)	1	(0.2)	2	(0.2)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Angioedema	血管浮腫	0	(0.0)	1	(0.2)	1	(0.1)
Pruritus	そう痒症	1	(0.2)	0	(0.0)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Vascular disorders	**血管障害**	**11**	**(1.9)**	**10**	**(1.6)**	**21**	**(1.8)**
Bleeding varicose vein	出血性静脈瘤	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	低血圧	10	(1.7)	9	(1.5)	19	(1.6)
Vasculitis	血管炎	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 82

表 2.7.4.8-28 投与中止に至った TEAE〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q4（5314pg/mL 超）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		616		584		1,200	
with one or more adverse events leading to treatment discontinuation		49	(8.0)	51	(8.7)	100	(8.3)
with no adverse events leading to treatment discontinuation		567	(92.0)	533	(91.3)	1,100	(91.7)
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**3**	**(0.5)**	**0**	**(0.0)**	**3**	**(0.3)**
Anaemia	貧血	2	(0.3)	0	(0.0)	2	(0.2)
Pancytopenia	汎血球減少症	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac disorders	**心臓障害**	**2**	**(0.3)**	**6**	**(1.0)**	**8**	**(0.7)**
Angina pectoris	狭心症	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure	心不全	2	(0.3)	2	(0.3)	4	(0.3)
Cardiac failure acute	急性心不全	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure chronic	慢性心不全	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure congestive	うっ血性心不全	0	(0.0)	1	(0.2)	1	(0.1)
Cardiogenic shock	心原性ショック	0	(0.0)	1	(0.2)	1	(0.1)
Gastrointestinal disorders	**胃腸障害**	**2**	**(0.3)**	**5**	**(0.9)**	**7**	**(0.6)**
Abdominal pain upper	上腹部痛	0	(0.0)	1	(0.2)	1	(0.1)
Dyspepsia	消化不良	0	(0.0)	1	(0.2)	1	(0.1)
Faecaloma	糞塊	0	(0.0)	1	(0.2)	1	(0.1)
Melaena	メレナ	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	悪心	1	(0.2)	0	(0.0)	1	(0.1)
Odynophagia	嚥下痛	1	(0.2)	0	(0.0)	1	(0.1)
Oesophageal achalasia	食道アカラシア	0	(0.0)	1	(0.2)	1	(0.1)
Peptic ulcer	消化性潰瘍	0	(0.0)	1	(0.2)	1	(0.1)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Fatigue	疲労	1	(0.2)	1	(0.2)	2	(0.2)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Immune system disorders	**免疫系障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Amyloidosis	アミロイドーシス	1	(0.2)	0	(0.0)	1	(0.1)
Infections and infestations	**感染症および寄生虫症**	**3**	**(0.5)**	**4**	**(0.7)**	**7**	**(0.6)**
Cellulitis	蜂巣炎	0	(0.0)	1	(0.2)	1	(0.1)
Disseminated tuberculosis	播種性結核	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonia	肺炎	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory tract infection	気道感染	1	(0.2)	0	(0.0)	1	(0.1)
Salmonella bacteraemia	サルモネラ性菌血症	0	(0.0)	1	(0.2)	1	(0.1)
Sepsis	敗血症	1	(0.2)	0	(0.0)	1	(0.1)
Urinary tract infection	尿路感染	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.3)**
Fall	転倒	0	(0.0)	1	(0.2)	1	(0.1)
Femur fracture	大腿骨骨折	1	(0.2)	0	(0.0)	1	(0.1)
Rib fracture	肋骨骨折	0	(0.0)	1	(0.2)	1	(0.1)
Subdural haematoma	硬膜下血腫	0	(0.0)	1	(0.2)	1	(0.1)
Thermal burn	熱傷	0	(0.0)	1	(0.2)	1	(0.1)
Wound secretion	創部分泌	0	(0.0)	1	(0.2)	1	(0.1)
Investigations	**臨床検査**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.3)**
Blood creatinine increased	血中クレアチニン増加	2	(0.3)	0	(0.0)	2	(0.2)
Liver function test increased	肝機能検査値上昇	0	(0.0)	1	(0.2)	1	(0.1)
Metabolism and nutrition disorders	**代謝および栄養障害**	**3**	**(0.5)**	**3**	**(0.5)**	**6**	**(0.5)**
Decreased appetite	食欲減退	2	(0.3)	0	(0.0)	2	(0.2)
Dehydration	脱水	0	(0.0)	1	(0.2)	1	(0.1)
Fluid overload	水分過負荷	0	(0.0)	1	(0.2)	1	(0.1)
Gout	痛風	0	(0.0)	1	(0.2)	1	(0.1)
Hyponatraemia	低ナトリウム血症	0	(0.0)	1	(0.2)	1	(0.1)
Metabolic acidosis	代謝性アシドーシス	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl	**良性、悪性および詳細不明の新生物**	**1**	**(0.2)**	**3**	**(0.5)**	**4**	**(0.3)**

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
cysts and polyps)	**（嚢胞およびポリープを含む）**						
Hepatic neoplasm	肝新生物	0	(0.0)	1	(0.2)	1	(0.1)
Lung neoplasm malignant	肺の悪性新生物	0	(0.0)	1	(0.2)	1	(0.1)
Metastases to lymph nodes	リンパ節転移	0	(0.0)	1	(0.2)	1	(0.1)
Plasmacytoma	形質細胞腫	0	(0.0)	1	(0.2)	1	(0.1)
Squamous cell carcinoma of head and neck	頭頚部扁平上皮癌	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**神経系障害**	**2**	**(0.3)**	**8**	**(1.4)**	**10**	**(0.8)**
Dizziness	浮動性めまい	1	(0.2)	1	(0.2)	2	(0.2)
Dysarthria	構語障害	0	(0.0)	1	(0.2)	1	(0.1)
Generalised tonic-clonic seizure	全身性強直性間代性発作	0	(0.0)	1	(0.2)	1	(0.1)
Headache	頭痛	0	(0.0)	1	(0.2)	1	(0.1)
Ischaemic stroke	虚血性脳卒中	1	(0.2)	0	(0.0)	1	(0.1)
Metabolic encephalopathy	代謝性脳症	0	(0.0)	1	(0.2)	1	(0.1)
Syncope	失神	0	(0.0)	3	(0.5)	3	(0.3)
Psychiatric disorders	**精神障害**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Mental status changes	精神状態変化	0	(0.0)	1	(0.2)	1	(0.1)
Renal and urinary disorders	**腎および尿路障害**	**12**	**(1.9)**	**16**	**(2.7)**	**28**	**(2.3)**
Acute kidney injury	急性腎障害	4	(0.6)	2	(0.3)	6	(0.5)
Chronic kidney disease	慢性腎臓病	3	(0.5)	8	(1.4)	11	(0.9)
Nephropathy	腎症	1	(0.2)	0	(0.0)	1	(0.1)
Renal failure	腎不全	3	(0.5)	5	(0.9)	8	(0.7)
Renal impairment	腎機能障害	1	(0.2)	1	(0.2)	2	(0.2)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Acute pulmonary oedema	急性肺水腫	1	(0.2)	0	(0.0)	1	(0.1)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**3**	**(0.5)**	**2**	**(0.3)**	**5**	**(0.4)**
Pruritus	そう痒症	2	(0.3)	0	(0.0)	2	(0.2)
Rash	発疹	1	(0.2)	1	(0.2)	2	(0.2)
Rash generalised	全身性皮疹	0	(0.0)	1	(0.2)	1	(0.1)

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Rash pruritic	そう痒性皮疹	1	(0.2)	0	(0.0)	1	(0.1)
Vascular disorders	**血管障害**	**15**	**(2.4)**	**7**	**(1.2)**	**22**	**(1.8)**
Haematoma	血腫	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	低血圧	15	(2.4)	6	(1.0)	21	(1.8)
Shock haemorrhagic	出血性ショック	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 83

表 2.7.4.8-29 注目すべき有害事象：症候性低血圧及び失神〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q1（1556pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Difference in % vs Placebo	
	n	(%)	n	(%)	Estimate (95% CI)†	p-value†
Subjects in population	599		604			
with one or more Syncope or Symptomatic Hypotension adverse events	64	(10.7)	68	(11.3)	-0.6 (-4.1, 3.0)	0.750
with no Syncope or Symptomatic Hypotension adverse events	535	(89.3)	536	(88.7)	0.6 (-3.0, 4.1)	0.750
Symptomatic Hypotension	47	(7.8)	46	(7.6)	0.2 (-2.8, 3.3)	0.881
Syncope	22	(3.7)	26	(4.3)	-0.6 (-2.9, 1.6)	0.576

† Based on Miettinen & Nurminen method.
Every subject is counted a single time for each applicable row and column.
Estimated differences, confidence intervals and p-values are provided in accordance with the statistical analysis plan.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 84

表 2.7.4.8-30 注目すべき有害事象：症候性低血圧及び失神〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q2（1556pg/mL 超 2816pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Difference in % vs Placebo	
	n	(%)	n	(%)	Estimate (95% CI)†	p-value†
Subjects in population	613		588			
with one or more Syncope or Symptomatic Hypotension adverse events	94	(15.3)	60	(10.2)	5.1 (1.4, 8.9)	0.008
with no Syncope or Symptomatic Hypotension adverse events	519	(84.7)	528	(89.8)	-5.1 (-8.9, -1.4)	0.008
Symptomatic Hypotension	70	(11.4)	45	(7.7)	3.8 (0.4, 7.1)	0.027
Syncope	28	(4.6)	19	(3.2)	1.3 (-0.9, 3.6)	0.233

† Based on Miettinen & Nurminen method.
Every subject is counted a single time for each applicable row and column.
Estimated differences, confidence intervals and p-values are provided in accordance with the statistical analysis plan.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 85

表 2.7.4.8-31 注目すべき有害事象：症候性低血圧及び失神〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q3（2816pg/mL 超 5314pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Difference in % vs Placebo	
	n	(%)	n	(%)	Estimate (95% CI)†	p-value†
Subjects in population	586		611			
with one or more Syncope or Symptomatic Hypotension adverse events	82	(14.0)	54	(8.8)	5.2 (1.6, 8.8)	0.005
with no Syncope or Symptomatic Hypotension adverse events	504	(86.0)	557	(91.2)	-5.2 (-8.8, -1.6)	0.005
Symptomatic Hypotension	57	(9.7)	40	(6.5)	3.2 (0.1, 6.4)	0.044
Syncope	27	(4.6)	17	(2.8)	1.8 (-0.3, 4.1)	0.094

† Based on Miettinen & Nurminen method.
Every subject is counted a single time for each applicable row and column.
Estimated differences, confidence intervals and p-values are provided in accordance with the statistical analysis plan.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 86

表 2.7.4.8-32 注目すべき有害事象：症候性低血圧及び失神〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q4（5314pg/mL 超）の被験者集団、主解析のカットオフまでのデータ〕

	Vericiguat		Placebo		Difference in % vs Placebo	
	n	(%)	n	(%)	Estimate (95% CI)†	p-value†
Subjects in population	616		584			
with one or more Syncope or Symptomatic Hypotension adverse events	59	(9.6)	69	(11.8)	-2.2 (-5.8, 1.3)	0.210
with no Syncope or Symptomatic Hypotension adverse events	557	(90.4)	515	(88.2)	2.2 (-1.3, 5.8)	0.210
Symptomatic Hypotension	44	(7.1)	53	(9.1)	-1.9 (-5.1, 1.2)	0.220
Syncope	21	(3.4)	21	(3.6)	-0.2 (-2.4, 2.0)	0.860

† Based on Miettinen & Nurminen method.
Every subject is counted a single time for each applicable row and column.
Estimated differences, confidence intervals and p-values are provided in accordance with the statistical analysis plan.
Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 87

表 2.7.4.8-33 肝臓関連事象〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q1（1556pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		599		604		1,203	
with one or more hepatic adverse events		2	(0.3)	5	(0.8)	7	(0.6)
with no hepatic adverse events		597	(99.7)	599	(99.2)	1,196	(99.4)
Hepatic ECI		**2**	**(0.3)**	**5**	**(0.8)**	**7**	**(0.6)**
Acute hepatic failure	急性肝不全	0	(0.0)	1	(0.2)	1	(0.1)
Hepatic enzyme increased	肝酵素上昇	1	(0.2)	1	(0.2)	2	(0.2)
Hepatic function abnormal	肝機能異常	0	(0.0)	1	(0.2)	1	(0.1)
Hepatitis acute	急性肝炎	1	(0.2)	0	(0.0)	1	(0.1)
Ischaemic hepatitis	虚血性肝炎	0	(0.0)	1	(0.2)	1	(0.1)
Liver function test increased	肝機能検査値上昇	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 88

表 2.7.4.8-34 肝臓関連事象〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q2（1556pg/mL 超 2816pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		613		588		1,201	
with one or more hepatic adverse events		6	(1.0)	2	(0.3)	8	(0.7)
with no hepatic adverse events		607	(99.0)	586	(99.7)	1,193	(99.3)
Hepatic ECI		**6**	**(1.0)**	**2**	**(0.3)**	**8**	**(0.7)**
Hepatic congestion	肝臓うっ血	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic enzyme increased	肝酵素上昇	2	(0.3)	1	(0.2)	3	(0.2)
Hepatic function abnormal	肝機能異常	1	(0.2)	1	(0.2)	2	(0.2)
Liver function test abnormal	肝機能検査異常	1	(0.2)	0	(0.0)	1	(0.1)
Liver injury	肝損傷	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 89

表 2.7.4.8-35 肝臓関連事象〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q3（2816pg/mL 超 5314pg/mL 以下）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		586		611		1,197	
with one or more hepatic adverse events		6	(1.0)	4	(0.7)	10	(0.8)
with no hepatic adverse events		580	(99.0)	607	(99.3)	1,187	(99.2)
Hepatic ECI		**6**	**(1.0)**	**4**	**(0.7)**	**10**	**(0.8)**
Acute hepatic failure	急性肝不全	0	(0.0)	2	(0.3)	2	(0.2)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1	(0.2)	1	(0.2)	2	(0.2)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1	(0.2)	1	(0.2)	2	(0.2)
Blood bilirubin increased	血中ビリルビン増加	1	(0.2)	1	(0.2)	2	(0.2)
Hepatic enzyme increased	肝酵素上昇	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic function abnormal	肝機能異常	0	(0.0)	1	(0.2)	1	(0.1)
Ischaemic hepatitis	虚血性肝炎	2	(0.3)	0	(0.0)	2	(0.2)
Liver function test increased	肝機能検査値上昇	1	(0.2)	0	(0.0)	1	(0.1)
Liver injury	肝損傷	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 90

表 2.7.4.8-36 肝臓関連事象〔試験 16493、ASaT 集団、ベースラインの NT-proBNP 値が Q4（5314pg/mL 超）の被験者集団、主解析のカットオフまでのデータ〕

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		616		584		1,200	
with one or more hepatic adverse events		9	(1.5)	2	(0.3)	11	(0.9)
with no hepatic adverse events		607	(98.5)	582	(99.7)	1,189	(99.1)
Hepatic ECI		**9**	**(1.5)**	**2**	**(0.3)**	**11**	**(0.9)**
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1	(0.2)	0	(0.0)	1	(0.1)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1	(0.2)	0	(0.0)	1	(0.1)
Blood bilirubin increased	血中ビリルビン増加	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic congestion	肝臓うっ血	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic enzyme abnormal	肝酵素異常	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic enzyme increased	肝酵素上昇	2	(0.3)	1	(0.2)	3	(0.3)
Hepatitis toxic	中毒性肝炎	0	(0.0)	1	(0.2)	1	(0.1)
Ischaemic hepatitis	虚血性肝炎	1	(0.2)	0	(0.0)	1	(0.1)
Liver function test abnormal	肝機能検査異常	1	(0.2)	0	(0.0)	1	(0.1)
Liver injury	肝損傷	1	(0.2)	0	(0.0)	1	(0.1)
Multiple organ dysfunction syndrome	多臓器機能不全症候群	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 91

表 2.7.4.8-37 QTcF 延長がみられた被験者の割合〔試験 16493、ASaT 集団（心電図検査で特定の所見が認められた被験者を除く）、主解析のカットオフまでのデータ〕

Visit	QTcF	Vericiguat (N=1101) n / m (%)	Placebo (N=1051) n / m (%)	Total (N=2152) n / m (%)
Baseline	Value > 450 msec	425 / 1087 (39.1)	396 / 1033 (38.3)	821 / 2120 (38.7)
	Value > 480 msec	162 / 1087 (14.9)	135 / 1033 (13.1)	297 / 2120 (14.0)
	Value > 500 msec	78 / 1087 (7.2)	72 / 1033 (7.0)	150 / 2120 (7.1)
Week 16	Value > 450 msec	348 / 942 (36.9)	345 / 899 (38.4)	693 / 1841 (37.6)
	Value > 480 msec	144 / 942 (15.3)	124 / 899 (13.8)	268 / 1841 (14.6)
	Value > 500 msec	69 / 942 (7.3)	61 / 899 (6.8)	130 / 1841 (7.1)
	CFB > 30 msec	131 / 934 (14.0)	127 / 889 (14.3)	258 / 1823 (14.2)
	CFB > 60 msec	54 / 934 (5.8)	39 / 889 (4.4)	93 / 1823 (5.1)
Discontinuation Visit	Value > 450 msec	14 / 30 (46.7)	10 / 27 (37.0)	24 / 57 (42.1)
	Value > 480 msec	5 / 30 (16.7)	4 / 27 (14.8)	9 / 57 (15.8)
	Value > 500 msec	3 / 30 (10.0)	3 / 27 (11.1)	6 / 57 (10.5)

Discontinuation Visit refers to premature discontinuation from treatment.

N=Number of treated subjects.

n/m=Number of subjects meeting the given criteria/Number of subjects with an ECG at the given visit or timeframe

CFB=Change from baseline.

QTcF: QT interval corrected per Fridericia′s Correction Formula

Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug.

Subjects who had any of the following ECG findings at baseline were excluded: Paced atrial and ventricular rhythm, Paced rhythm, Paced ventricular rhythm, Atrial fibrillation, Atrial flutter, Right bundle branch block, Left bundle branch block, Pre-excitation

Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 92

表 2.7.4.8-38 トルサード ド ポアント／QT 延長（SMQ）（狭域検索用語）の発現割合（試験 16493、ASaT 集団、主解析のカットオフまでのデータ）

		Vericiguat		Placebo		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		2,519		2,515		5,034	
with one or more adverse events		42	(1.7)	65	(2.6)	107	(2.1)
with no adverse event		2,477	(98.3)	2,450	(97.4)	4,927	(97.9)
Cardiac disorders	**心臓障害**	**42**	**(1.7)**	**60**	**(2.4)**	**102**	**(2.0)**
Ventricular tachycardia	心室性頻脈	42	(1.7)	60	(2.4)	102	(2.0)
Investigations	**臨床検査**	**0**	**(0.0)**	**6**	**(0.2)**	**6**	**(0.1)**
Electrocardiogram QT prolonged	心電図ＱＴ延長	0	(0.0)	6	(0.2)	6	(0.1)

Every subject is counted a single time for each applicable row and column.
Note: Includes events from the day of first dose of study drug to 14 days after the last dose of study drug.
Based on data up to the primary completion date (18Jun2019).

Source: 5.3.5.1.6 16493_Additional analysis/Table 93

2.7.5　参考文献

2.7 臨床概要における参考文献の掲載先を以下に示す。

2.7.1 生物薬剤学試験及び関連する分析法；「参考文献一覧」の項

2.7.2 臨床薬理試験；「参考文献一覧」の項

2.7.3 臨床的有効性；「参考文献一覧」の項

2.7.4 臨床的安全性；「参考文献一覧」の項