

APPENDIX

Beta2-agonist/Corticosteroid Therapy in Chronic Obstructive Pulmonary Disease Patients at High Cardiac Risk

ONLINE TABLE 1 Number of Subjects with On-treatment Cardiovascular Adverse Events of Special Interest (using Standardized MedDRA Queries [SMQs])

Subgroup	Placebo	FF 100	VI 25	FF/VI 100/25
Preferred term	n = 4,131	n = 4,157	n = 4,140	n = 4,140
<hr/>				
Any cardiac effect (SMQ grouping)				
Any event	695 (17%)	699 (17%)	707 (17%)	735 (18%)
Cardiac arrhythmias (SMQ)				
Any event	211 (5%)	229 (6%)	224 (5%)	209 (5%)
Atrial fibrillation	55 (1%)	66 (2%)	60 (1%)	68 (2%)
Syncope	16 (<1%)	27 (<1%)	22 (<1%)	25 (<1%)
Tachycardia	22 (<1%)	21 (<1%)	18 (<1%)	19 (<1%)
Sudden death	20 (<1%)	14 (<1%)	17 (<1%)	20 (<1%)
Palpitations	23 (<1%)	18 (<1%)	15 (<1%)	13 (<1%)
Arrhythmia	11 (<1%)	16 (<1%)	11 (<1%)	15 (<1%)
Cardio-respiratory arrest	11 (<1%)	9 (<1%)	11 (<1%)	5 (<1%)
Atrial flutter	13 (<1%)	10 (<1%)	6 (<1%)	5 (<1%)

Cardiac arrest	9 (<1%)	10 (<1%)	11 (<1%)	4 (<1%)
Ventricular extrasystoles	9 (<1%)	8 (<1%)	9 (<1%)	8 (<1%)
Bradycardia	9 (<1%)	4 (<1%)	7 (<1%)	8 (<1%)
Sinus tachycardia	4 (<1%)	7 (<1%)	8 (<1%)	5 (<1%)
Sudden cardiac death	3 (<1%)	7 (<1%)	6 (<1%)	1 (<1%)
Supraventricular extrasystoles	3 (<1%)	3 (<1%)	5 (<1%)	6 (<1%)
Ventricular tachycardia	0	5 (<1%)	3 (<1%)	7 (<1%)
Loss of consciousness	3 (<1%)	3 (<1%)	3 (<1%)	4 (<1%)
Atrioventricular block complete	3 (<1%)	2 (<1%)	3 (<1%)	3 (<1%)
Bundle branch block right	3 (<1%)	2 (<1%)	3 (<1%)	3 (<1%)
Sinus node dysfunction	3 (<1%)	2 (<1%)	3 (<1%)	3 (<1%)
Bundle branch block left	1 (<1%)	2 (<1%)	4 (<1%)	3 (<1%)
Atrioventricular block second degree	1 (<1%)	4 (<1%)	3 (<1%)	1 (<1%)
Heart rate increased	2 (<1%)	2 (<1%)	1 (<1%)	4 (<1%)
Sinus bradycardia	0	2 (<1%)	3 (<1%)	4 (<1%)
Extrasystoles	3 (<1%)	3 (<1%)	1 (<1%)	1 (<1%)
Supraventricular tachycardia	2 (<1%)	2 (<1%)	3 (<1%)	1 (<1%)
Arrhythmia supraventricular	3 (<1%)	1 (<1%)	2 (<1%)	1 (<1%)

Tachycardia paroxysmal	1 (<1%)	2 (<1%)	2 (<1%)	1 (<1%)
Atrioventricular block	1 (<1%)	2 (<1%)	1 (<1%)	1 (<1%)
Atrioventricular block first degree	0	1 (<1%)	2 (<1%)	2 (<1%)
Ventricular fibrillation	1 (<1%)	0	3 (<1%)	1 (<1%)
Atrial tachycardia	1 (<1%)	0	0	3 (<1%)
Bradycardia	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)
Tachycardia	2 (<1%)	0	1 (<1%)	1 (<1%)
Ventricular arrhythmia	0	1 (<1%)	1 (<1%)	1 (<1%)
Adams-Stokes syndrome	1 (<1%)	1 (<1%)	0	0
Cardiac fibrillation	1 (<1%)	0	0	1 (<1%)
Heart rate decreased	1 (<1%)	1 (<1%)	0	0
Heart rate irregular	0	1 (<1%)	0	1 (<1%)
Sinoatrial block	0	1 (<1%)	1 (<1%)	0
Sinus arrhythmia	0	0	0	2 (<1%)
Bifascicular block	0	0	1 (<1%)	0
Bundle branch block	0	1 (<1%)	0	0
Cardiac death	0	0	1 (<1%)	0
Conduction disorder	1 (<1%)	0	0	0

Defect conduction intraventricular	0	0	0	1 (<1%)
Electrocardiogram P wave abnormal	0	0	1 (<1%)	0
Electrocardiogram QT prolonged	0	1 (<1%)	0	0
Electrocardiogram repolarisation abnormality	0	0	1 (<1%)	0
Paroxysmal arrhythmia	1 (<1%)	0	0	0
Pulseless electrical activity	0	0	1 (<1%)	0
Supraventricular tachyarrhythmia	1 (<1%)	0	0	0
Hypertension (SMQ)				
Any event	204 (5%)	212 (5%)	203 (5%)	236 (6%)
Hypertension	136 (3%)	144 (3%)	132 (3%)	160 (4%)
Blood pressure increased	39 (<1%)	41 (<1%)	44 (1%)	43 (1%)
Hypertensive crisis	23 (<1%)	26 (<1%)	18 (<1%)	31 (<1%)
Hypertensive heart disease	2 (<1%)	3 (<1%)	4 (<1%)	0
Accelerated hypertension	2 (<1%)	2 (<1%)	1 (<1%)	0
Blood pressure fluctuation	3 (<1%)	1 (<1%)	0	1 (<1%)
Hypertensive emergency	2 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)
Blood pressure inadequately controlled	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)
Labile blood pressure	0	0	3 (<1%)	1 (<1%)

Blood pressure systolic increased	2 (<1%)	0	0	1 (<1%)
Labile hypertension	0	0	0	3 (<1%)
Essential hypertension	0	0	1 (<1%)	1 (<1%)
Blood pressure diastolic increased	0	0	0	1 (<1%)
Hypertensive angiopathy	0	1 (<1%)	0	0
Hypertensive cardiomyopathy	0	0	1 (<1%)	0
Metabolic syndrome	0	0	1 (<1%)	0
Renovascular hypertension	0	0	1 (<1%)	0
Secondary hypertension	0	1 (<1%)	0	0
Cardiac failure (SMQ)				
Any event	194 (5%)	157 (4%)	173 (4%)	188 (5%)
Oedema peripheral	46 (1%)	36 (<1%)	58 (1%)	31 (<1%)
Cardiac failure congestive	45 (1%)	39 (<1%)	29 (<1%)	48 (1%)
Cardiac failure	43 (1%)	30 (<1%)	28 (<1%)	44 (1%)
Peripheral swelling	11 (<1%)	12 (<1%)	13 (<1%)	20 (<1%)
Cardiac failure chronic	11 (<1%)	13 (<1%)	8 (<1%)	13 (<1%)
Edema	9 (<1%)	10 (<1%)	10 (<1%)	5 (<1%)
Lower respiratory tract congestion	5 (<1%)	7 (<1%)	4 (<1%)	7 (<1%)

Cardiac failure acute	7 (<1%)	3 (<1%)	3 (<1%)	7 (<1%)
Pulmonary congestion	4 (<1%)	3 (<1%)	9 (<1%)	3 (<1%)
Pulmonary edema	3 (<1%)	5 (<1%)	6 (<1%)	4 (<1%)
Cor pulmonale	7 (<1%)	6 (<1%)	2 (<1%)	2 (<1%)
Left ventricular failure	4 (<1%)	5 (<1%)	1 (<1%)	4 (<1%)
Cardiopulmonary failure	1 (<1%)	3 (<1%)	4 (<1%)	4 (<1%)
Left ventricular dysfunction	2 (<1%)	1 (<1%)	2 (<1%)	4 (<1%)
Acute pulmonary edema	3 (<1%)	1 (<1%)	1 (<1%)	3 (<1%)
Acute left ventricular failure	1 (<1%)	1 (<1%)	2 (<1%)	2 (<1%)
Diastolic dysfunction	1 (<1%)	1 (<1%)	2 (<1%)	1 (<1%)
Cardiogenic shock	2 (<1%)	1 (<1%)	1 (<1%)	0
Cardiomegaly	1 (<1%)	0	1 (<1%)	1 (<1%)
Right ventricular failure	1 (<1%)	1 (<1%)	0	1 (<1%)
Ejection fraction decreased	1 (<1%)	0	0	1 (<1%)
Orthopnea	0	1 (<1%)	0	1 (<1%)
Brain natriuretic peptide increased	1 (<1%)	0	0	0
Cor pulmonale acute	0	0	1 (<1%)	0
Cor pulmonale chronic	0	1 (<1%)	0	0

Hepatic congestion	0	0	1 (<1%)	0
Edema due to cardiac disease	0	0	0	1 (<1%)
Ventricular failure	0	1 (<1%)	0	0
Ischemic heart disease (SMQ)				
Any event	163 (4%)	153 (4%)	165 (4%)	156 (4%)
Angina pectoris	46 (1%)	41 (<1%)	49 (1%)	28 (<1%)
Coronary artery disease	30 (<1%)	23 (<1%)	38 (<1%)	32 (<1%)
Myocardial infarction	24 (<1%)	32 (<1%)	27 (<1%)	24 (<1%)
Angina unstable	28 (<1%)	25 (<1%)	18 (<1%)	25 (<1%)
Acute myocardial infarction	24 (<1%)	20 (<1%)	21 (<1%)	28 (<1%)
Myocardial ischemia	11 (<1%)	13 (<1%)	9 (<1%)	16 (<1%)
Acute coronary syndrome	3 (<1%)	3 (<1%)	6 (<1%)	5 (<1%)
Ischemic cardiomyopathy	4 (<1%)	4 (<1%)	4 (<1%)	2 (<1%)
Arteriosclerosis coronary artery	5 (<1%)	2 (<1%)	1 (<1%)	3 (<1%)
Coronary artery stenosis	2 (<1%)	2 (<1%)	4 (<1%)	3 (<1%)
Coronary artery occlusion	2 (<1%)	1 (<1%)	3 (<1%)	0
Vascular graft occlusion	1 (<1%)	1 (<1%)	1 (<1%)	0
Coronary artery thrombosis	1 (<1%)	0	1 (<1%)	0

Coronary ostial stenosis	1 (<1%)	0	0	1 (<1%)
Electrocardiogram T wave abnormal	1 (<1%)	0	0	1 (<1%)
Troponin increased	0	0	0	2 (<1%)
Coronary angioplasty	0	0	1 (<1%)	0
Coronary artery insufficiency	0	0	1 (<1%)	0
Coronary artery restenosis	0	0	0	1 (<1%)
Coronary vascular graft occlusion	0	1 (<1%)	0	0
Myocardial necrosis	0	0	0	1 (<1%)
Myocardial necrosis marker increased	1 (<1%)	0	0	0
Troponin I increased	0	0	1 (<1%)	0

Central nervous system hemorrhages and
cerebrovascular conditions (SMQ)

Any event	90 (2%)	95 (2%)	97 (2%)	101 (2%)
Ischemic stroke	19 (<1%)	16 (<1%)	15 (<1%)	19 (<1%)
Transient ischemic attack	12 (<1%)	20 (<1%)	23 (<1%)	13 (<1%)
Cerebrovascular accident	16 (<1%)	12 (<1%)	13 (<1%)	19 (<1%)
Carotid artery stenosis	11 (<1%)	12 (<1%)	7 (<1%)	11 (<1%)
Cerebral infarction	5 (<1%)	8 (<1%)	6 (<1%)	8 (<1%)

Vascular encephalopathy	5 (<1%)	3 (<1%)	5 (<1%)	4 (<1%)
Hemorrhagic stroke	4 (<1%)	4 (<1%)	4 (<1%)	3 (<1%)
Cerebrovascular disorder	5 (<1%)	4 (<1%)	3 (<1%)	2 (<1%)
Carotid arteriosclerosis	2 (<1%)	4 (<1%)	1 (<1%)	3 (<1%)
Carotid artery occlusion	2 (<1%)	2 (<1%)	1 (<1%)	3 (<1%)
Cerebral arteriosclerosis	2 (<1%)	1 (<1%)	3 (<1%)	2 (<1%)
Cerebral hemorrhage	2 (<1%)	0	3 (<1%)	3 (<1%)
Lacunar infarction	1 (<1%)	2 (<1%)	2 (<1%)	2 (<1%)
Subarachnoid hemorrhage	1 (<1%)	2 (<1%)	3 (<1%)	1 (<1%)
Vertebrobasilar insufficiency	1 (<1%)	0	3 (<1%)	3 (<1%)
Cerebral ischemia	2 (<1%)	2 (<1%)	0	2 (<1%)
Subdural hematoma	0	1 (<1%)	2 (<1%)	3 (<1%)
Cerebrovascular insufficiency	0	0	3 (<1%)	2 (<1%)
Ischemic cerebral infarction	2 (<1%)	0	2 (<1%)	0
Brain injury	1 (<1%)	0	1 (<1%)	1 (<1%)
Hypoxic-ischemic encephalopathy	1 (<1%)	0	1 (<1%)	1 (<1%)
Intracranial aneurysm	1 (<1%)	1 (<1%)	0	1 (<1%)
Vertebral artery stenosis	1 (<1%)	1 (<1%)	0	1 (<1%)

Aphasia	0	1 (<1%)	1 (<1%)	0
Carotid artery aneurysm	1 (<1%)	1 (<1%)	0	0
Carotid artery disease	1 (<1%)	0	0	1 (<1%)
Dysarthria	0	1 (<1%)	1 (<1%)	0
Hemiparesis	0	0	0	2 (<1%)
Intraventricular hemorrhage	0	0	2 (<1%)	0
Subclavian steal syndrome	1 (<1%)	1 (<1%)	0	0
Amaurosis fugax	0	1 (<1%)	0	0
Basal ganglia infarction	0	0	1 (<1%)	0
Basilar artery occlusion	0	0	0	1 (<1%)
Brachiocephalic artery stenosis	1 (<1%)	0	0	0
Brain stem infarction	0	0	0	1 (<1%)
Brain stem ischemia	0	1 (<1%)	0	0
Brain stem stroke	1 (<1%)	0	0	0
Cerebral artery thrombosis	0	0	1 (<1%)	0
Cerebral hematoma	0	0	1 (<1%)	0
Diplegia	0	1 (<1%)	0	0
Hemorrhage intracranial	0	1 (<1%)	0	0

Hemorrhagic cerebral infarction	1 (<1%)	0	0	0
Hemiplegia	0	1 (<1%)	0	0
Paresis	1 (<1%)	0	0	0
Retinal artery occlusion	1 (<1%)	0	0	0
Ruptured cerebral aneurism	0	0	1 (<1%)	0

FF = fluticasone furoate, VI = vilanterol.

ONLINE TABLE 2 Number of Subjects with On-treatment Cardiovascular Serious Adverse Events of Special Interest (using SMQs)

Subgroup	Placebo	FF 100	VI 25	FF/VI 100/25
Preferred term	n = 4,131	n = 4,157	n = 4,140	n = 4,140
<hr/>				
Any cardiovascular effect (SMQ grouping)				
Any event	318 (8%)	320 (8%)	337 (8%)	350 (8%)
Ischemic heart disease (SMQ)				
Any event	124 (3%)	120 (3%)	121 (3%)	122 (3%)
Myocardial infarction	24 (<1%)	32 (<1%)	26 (<1%)	24 (<1%)
Acute myocardial infarction	23 (<1%)	20 (<1%)	21 (<1%)	28 (<1%)
Coronary artery disease	22 (<1%)	14 (<1%)	25 (<1%)	24 (<1%)
Angina unstable	23 (<1%)	22 (<1%)	16 (<1%)	23 (<1%)
Angina pectoris	22 (<1%)	19 (<1%)	20 (<1%)	12 (<1%)
Myocardial ischaemia	7 (<1%)	8 (<1%)	5 (<1%)	7 (<1%)
Acute coronary syndrome	3 (<1%)	3 (<1%)	6 (<1%)	5 (<1%)
Ischemic cardiomyopathy	4 (<1%)	3 (<1%)	4 (<1%)	1 (<1%)
Arteriosclerosis coronary artery	3 (<1%)	1 (<1%)	1 (<1%)	3 (<1%)

Coronary artery stenosis	1 (<1%)	2 (<1%)	1 (<1%)	2 (<1%)
Coronary artery occlusion	1 (<1%)	1 (<1%)	3 (<1%)	0
Coronary artery insufficiency	0	0	1 (<1%)	0
Coronary artery restenosis	0	0	0	1 (<1%)
Coronary artery thrombosis	0	0	1 (<1%)	0
Coronary ostial stenosis	0	0	0	1 (<1%)
Coronary vascular graft occlusion	0	1 (<1%)	0	0
Myocardial necrosis	0	0	0	1 (<1%)
Myocardial necrosis marker increased	1 (<1%)	0	0	0
Vascular graft occlusion	0	1 (<1%)	0	0

Cardiac arrhythmias (SMQ)

Any event	94 (2%)	92 (2%)	107 (3%)	93 (2%)
Atrial fibrillation	31 (<1%)	22 (<1%)	30 (<1%)	32 (<1%)
Sudden death	20 (<1%)	14 (<1%)	17 (<1%)	20 (<1%)
Cardio-respiratory arrest	11 (<1%)	9 (<1%)	11 (<1%)	5 (<1%)
Cardiac arrest	9 (<1%)	9 (<1%)	11 (<1%)	4 (<1%)
Syncope	6 (<1%)	7 (<1%)	6 (<1%)	10 (<1%)
Sudden cardiac death	3 (<1%)	7 (<1%)	6 (<1%)	1 (<1%)

Atrial flutter	6 (<1%)	3 (<1%)	3 (<1%)	3 (<1%)
Arrhythmia	1 (<1%)	4 (<1%)	3 (<1%)	6 (<1%)
Atrioventricular block complete	3 (<1%)	2 (<1%)	3 (<1%)	3 (<1%)
Bradycardia	3 (<1%)	1 (<1%)	1 (<1%)	3 (<1%)
Ventricular tachycardia	0	3 (<1%)	2 (<1%)	3 (<1%)
Sinus node dysfunction	3 (<1%)	2 (<1%)	0	2 (<1%)
Atrioventricular block second degree	1 (<1%)	2 (<1%)	3 (<1%)	0
Ventricular fibrillation	1 (<1%)	0	3 (<1%)	1 (<1%)
Atrioventricular block	0	2 (<1%)	1 (<1%)	1 (<1%)
Bradyarrhythmia	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)
Loss of consciousness	0	1 (<1%)	1 (<1%)	2 (<1%)
Ventricular extrasystoles	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)
Supraventricular tachycardia	0	0	3 (<1%)	0
Tachycardia	0	2 (<1%)	1 (<1%)	0
Adams-Stokes syndrome	1 (<1%)	1 (<1%)	0	0
Sinoatrial block	0	1 (<1%)	1 (<1%)	0
Sinus tachycardia	0	0	2 (<1%)	0
Arrhythmia supraventricular	0	0	3 (<1%)	0

Atrial tachycardia	0	0	0	1 (<1%)
Atrioventricular block first degree	0	1 (<1%)	0	0
Bundle branch block left	0	0	0	1 (<1%)
Bundle branch block right	0	0	0	1 (<1%)
Cardiac death	0	0	1 (<1%)	0
Conduction disorder	1 (<1%)	0	0	0
Extrasystoles	0	0	1 (<1%)	0
Pulseless electrical activity	0	0	1 (<1%)	0
Sinus bradycardia	0	0	0	1 (<1%)
Supraventricular extrasystoles	0	0	1 (<1%)	0
Supraventricular tachyarrhythmia	1 (<1%)	0	0	0
Tachycardia paroxysmal	0	0	0	1 (<1%)
Cardiac failure (SMQ)				
Any event	75 (2%)	66 (2%)	61 (1%)	83 (2%)
Cardiac failure congestive	26 (<1%)	26 (<1%)	1 (<1%)	230 (<1%)
Cardiac failure	28 (<1%)	17 (<1%)	19 (<1%)	28 (<1%)
Cardiac failure chronic	5 (<1%)	7 (<1%)	4 (<1%)	7 (<1%)
Cardiac failure acute	7 (<1%)	3 (<1%)	3 (<1%)	7 (<1%)

Pulmonary edema	2 (<1%)	4 (<1%)	4 (<1%)	3 (<1%)
Cardiopulmonary failure	1 (<1%)	3 (<1%)	4 (<1%)	4 (<1%)
Acute left ventricular failure	1 (<1%)	1 (<1%)	2 (<1%)	2 (<1%)
Acute pulmonary edema	2 (<1%)	1 (<1%)	1 (<1%)	2 (<1%)
Left ventricular failure	3 (<1%)	2 (<1%)	1 (<1%)	0
Cor pulmonale	1 (<1%)	2 (<1%)	0	2 (<1%)
Cardiogenic shock	2 (<1%)	1 (<1%)	1 (<1%)	0
Pulmonary congestion	0	1 (<1%)	3 (<1%)	0
Edema peripheral	0	2 (<1%)	0	1 (<1%)
Cardiomegaly	1 (<1%)	0	0	0
Diastolic dysfunction	0	1 (<1%)	0	0
Left ventricular dysfunction	0	0	1 (<1%)	0
Right ventricular failure	0	0	0	1 (<1%)

Central nervous system hemorrhages and
cerebrovascular conditions (SMQ)

Any event	66 (2%)	67 (2%)	68 (2%)	80 (2%)
Ischemic stroke	19 (<1%)	15 (<1%)	14 (<1%)	19 (<1%)
Cerebrovascular accident	16 (<1%)	11 (<1%)	11 (<1%)	18 (<1%)

Transient ischemic attack	7 (<1%)	13 (<1%)	16 (<1%)	9 (<1%)
Cerebral infarction	5 (<1%)	6 (<1%)	4 (<1%)	7 (<1%)
Carotid artery stenosis	4 (<1%)	6 (<1%)	4 (<1%)	7 (<1%)
Hemorrhagic stroke	4 (<1%)	4 (<1%)	4 (<1%)	3 (<1%)
Cerebral hemorrhage	2 (<1%)	0	3 (<1%)	3 (<1%)
Subarachnoid hemorrhage	1 (<1%)	2 (<1%)	3 (<1%)	1 (<1%)
Cerebrovascular disorder	2 (<1%)	1 (<1%)	0	1 (<1%)
Ischemic cerebral infarction	2 (<1%)	0	2 (<1%)	0
Lacunar infarction	0	1 (<1%)	1 (<1%)	2 (<1%)
Subdural hematoma	0	1 (<1%)	1 (<1%)	2 (<1%)
Vertebrobasilar insufficiency	1 (<1%)	0	1 (<1%)	2 (<1%)
Carotid artery occlusion	0	1 (<1%)	0	2 (<1%)
Cerebral ischemia	1 (<1%)	1 (<1%)	0	1 (<1%)
Vascular encephalopathy	0	1 (<1%)	0	2 (<1%)
Brain injury	0	0	1 (<1%)	1 (<1%)
Carotid artery aneurism	1 (<1%)	1 (<1%)	0	0
Cerebrovascular insufficiency	0	0	2 (<1%)	0
Hypoxic-ischaemic encephalopathy	1 (<1%)	0	0	1 (<1%)

Intracranial aneurism	0	1 (<1%)	0	1 (<1%)
Vertebral artery stenosis	1 (<1%)	0	0	1 (<1%)
Aphasia	0	0	1 (<1%)	0
Basal ganglia infarction	0	0	1 (<1%)	0
Basilar artery occlusion	0	0	0	1 (<1%)
Brain stem infarction	0	0	0	1 (<1%)
Brain stem ischemia	0	1 (<1%)	0	0
Brain stem stroke	1 (<1%)	0	0	0
Carotid arteriosclerosis	0	1 (<1%)	0	0
Carotid artery disease	0	0	0	1 (<1%)
Cerebral arteriosclerosis	0	0	1 (<1%)	0
Cerebral hematoma	0	0	1 (<1%)	0
Diplegia	0	1 (<1%)	0	0
Hemorrhage intracranial	0	1 (<1%)	0	0
Hemorrhagic cerebral infarction	1 (<1%)	0	0	0
Hemiparesis	0	0	0	1 (<1%)
Hemiplegia	0	1 (<1%)	0	0
Intraventricular hemorrhage	0	0	1 (<1%)	0

Retinal artery occlusion	1 (<1%)	0	0	0
Subclavian steal syndrome	1 (<1%)	0	0	0
Hypertension (SMQ)				
Any event	12 (<1%)	17 (<1%)	16 (<1%)	19 (<1%)
Hypertension	7 (<1%)	9 (<1%)	8 (<1%)	11 (<1%)
Hypertensive crisis	3 (<1%)	5 (<1%)	5 (<1%)	9 (<1%)
Hypertensive heart disease	0	1 (<1%)	2 (<1%)	0
Blood pressure increased	0	2 (<1%)	0	0
Hypertensive emergency	2 (<1%)	0	0	0
Renovascular hypertension	0	0	1 (<1%)	0
Secondary hypertension	0	1 (<1%)	0	0

FF = fluticasone furoate, VI = vilanterol.

ONLINE TABLE 3 Composition of Regions

Region	Countries
U.S.	U.S.
Asia	China, Indonesia, India, Japan, Korea, Malaysia, Philippines, Taiwan, Thailand, Vietnam
Europe 1 (EU)	Austria, Belgium, Bulgaria, Czech Republic, France, Germany, Greece, Hungary, Latvia, Netherlands, Poland, Romania, Slovakia, Spain, United Kingdom, Croatia
Europe 2 (Non-EU)	Bosnia and Herzegovina, Belarus, , Georgia, Israel, Macedonia (Former Yugoslav Republic of), Russian Federation, Serbia, Turkey, Ukraine
Rest of World	Argentina, Australia, Canada, Chile, Columbia, Mexico, , South Africa