The investigator reported that there was no reasonable possibility that the events C6 perched facette with a right C6 facette fracture, left thumb fracture, undisplaced C2 fracture and scalp laceration were related to the blinded investigational product.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	11-JAN-one year after*

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Atrial fibrillation	Atrial fibrillation (Atrial fibrillation)	07-FEB-one year after* (27 days)

Case Narrative : This 61 year old white male subject was participating in a LAPLACE TIMI 57 - double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and developed atrial fibrillation.

The subject's medical history included hypercholesterolemia, atrial fibrillation episode on 18/Dec/five years ago*, "thyreopathy", hypertensive disease, multilevel vertebrogenic "algic" syndrome, tonsillectomy, condition after surgery due to carpal tunnel syndrome, occasional alcohol use and ex-smoker. Previous treatment for the condition under study was not provided by the investigator at the time of this report. Concomitant medications included Statin (simvastatin), Anopyrin (acetylsalicylic acid), Prestarium Neo (perindopril arginine), Triglyx (atorvastatin calcium), Trexan (methotrexate) and folic acid.

The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 14/Nov/[redacted]. Approximately three months later, on 07/Feb/one year after*, the subject developed atrial fibrillation. On 08/Nov/same year*, the subject came to the hospital for his regular check-up visit and he reported palpitations that onset one day before. Additionally, the subject was diagnosed with infection of the upper respiratory tract. Upon admission, electrocardiogram showed irregular heart rate, recurrence of atrial fibrillation, ventricular response about 70/min, heart axis of 15 degrees, QRS of 0.10, QT of 0.38, ST at isoelectric line; flat negativity of T in lead III and transition zone at V3 and 4. Laboratory data showed sodium of 141, potassium of 4.15, chloride of 108, C-reactive protein of 1.9, white blood cell count of 7.7, red blood cell count of 5.00, B-hemoglobin of 162 and B-hematocrit of 0.47. Intravenous propafenone was administered with no effect and therefore, electrical defibrillation was carried out under short-term intravenous anesthesia. After cardioversion, electrocardiogram was performed and showed restored sinus rhythm with no sequelae, heart rate of 57/min, horizontal axis, transition zone V3, ST segment was oblique in the chest leads, otherwise it was isoelectric, flat negativity of T wave in lead III, negativity in V1, transmission intervals were normal. The sinus rhythm was restored and sinus rhythm persisted. Additional treatment medications included Spatizalex (atorvastatin calcium), Rytmonorm (propafenone hydrochloride) and Clexane (enoxaparin sodium). The event was reported to have resolved on 08/Feb/one year after* and the subject was discharged from the hospital on 09/Feb/one year after* with stable condition. The subject's last dose of blinded investigational product prior to the event was on 11/Jan/one year after*. The investigator reported that the subject completed the treatment according to the protocol.

The investigator reported that there was no reasonable possibility that the event atrial fibrillation was related to the blinded investigational product.

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ADDITIONAL INFORMATION RECEIVED ON 29/FEB/one year after*: The investigator reported that the subject was hospitalized from 18/Dec/five years ago* to 21/Dec five years ago* due to atrial fibrillation and the subject was treated with metoprolol and propafenone. The investigator stated that the subject did not receive previous treatment for the condition under study and there were no risk factors associated with the event.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	Yes	No	---	---	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
transitory ischaemic attack	Transient ischaemic attack (Transient ischaemic attack)	04-JAN-one year after*---

Case Narrative : This 62 years old Caucasian male was participating in a phase 2, randomized, double-blind, placebo and active controlled, dose-ranging, multiple-dose, parallel-group study to evaluate the LDL-C lowering properties of AMG 145, compared to placebo and ezetimibe when used as add-on therapy in dyslipidemic and experienced stroke.

The subjects medical history included hypercholesterolemia, chronic ischemic heart disease, status post diaphragmatic Q-myocardial infarction with recurrence in Apr/three years ago* that was managed by direct percutaneous transluminal angioplasty on the left marginal artery 2 and stent implantation, recurrence of diaphragmatic ST-elevation myocardial infarction (STEMI) on 09/Feb/two years ago*, coronary angiography, progression of stenosis on proximal portion of the left circumflex artery to 80%, new 95% lesion of proximal portion of the left marginal artery 2 (culprit), in-stent 70% re-stenosis, left ventricular dysfunction, percutaneous coronary intervention, grade 3 hypertension, hyperlipoproteinemia, metabolic syndrome, overweight and gout with history of repeated episodes. Previous treatment for the condition under study was not provided by the investigator at the time of this report. Concomitant medications included Anopyrin (acetylsalicylic acid), Preductal MR (trimetazidine hydrochloride), Betaloc (metoprolol tartrate), Prestarium combi (indapamide, perindopril), Lusopress (nitrendipine), Torvacard (atorvastatin), Magnesii lactici (magnesium lactate) and Apo-allopurinol (allopurinol).

The subject received the first dose of blinded investigational study product on 28/Nov/[redacted]. The following day, on 29/Nov/same year*, the subject underwent meniscus surgery. Reportedly approximately one month and one week after initiation of first dose, on 04/Jan/one year after*, the subject experienced intermittent left-sided limbs paresis due to a stroke. Three weeks later, on 20/Jan/one year after*, the subject experienced sudden headache which was described as migratory and was not permanent and reported paresthesia and weakness of left-sided limbs. On 25/Jan/one year after*, the subject presented to the hospital with complains of headache in frontal area. He did not report dizziness; vision and hearing were not impaired and weakness of limbs and paresthesia were not present. The subject was hospitalized on that same date. On admission vital signs included blood pressure of 150/80 mmHg and heart rate of 63 beats per minute. The subject underwent neurological examination which did not show focal lesion in central nervous system. A radiogram of heart and lungs revealed dilation of heart shadow in the left ventricle; otherwise normal finding in intrathoracic organs. A computed tomography of brain showed irregular hypodense focuses corresponding to postischemic changes on both periventricular parts an on the right occipital area. Evidence of hemorrhage and abnormal finding in the bone window were not seen. Chamber system and subarachnoid areas were not dilated. Structures in the medial line were not shifted. Depicted paranasal sinuses were free. Adequate pneumatization of mastoid processes was seen. A triplex ultrasound of carotid and vertebral arteries showed heterogenic

diffuse atherosclerotic changes in bifurcation and in both-sided internal carotid arteries in width up to 3.5-4.0 mm resulting in approximately 40% stenosis in the left internal carotid artery and approximately 30% stenosis in the right internal carotid artery. Vertebral arteries including branching of subclavian arteries on both sides were depicted. Width, flow direction and Doppler spectrums were normal on vertebral arteries bilaterally. Transcranial color coded sonography has shown impermeable T-window on both sides. The subjects antiplatelet therapy was switched to clopidogrel. The event was ongoing and the subject remained hospitalized at the time of this report. The subjects last dose of blinded investigational product was on 20/Jan/one year after*. Blinded investigational product was continued.

The investigator reported that there was not a reasonable possibility that the event stroke was related to the blinded investigational product.

ADDITIONAL INFORMATION RECEIVED ON 02/FEB/one year after*: Previous and current treatment for the condition under study included atorvastatin. The subject had family history of cerebral vascular accident. The event term was changed by investigator to "transitory" ischaemic attack. Laboratory tests revealed sodium 140, potassium 4.91, chloride 106, creatinine 94, alanine aminotransferase 0.36, aspartate aminotransferase 0.41, gamma-glutamyltransferase 0.44, high density lipoprotein 0.79, low density lipoprotein 1.83, glucose 5.5, white blood cell count 8.21, red blood cell count 4.71, hemoglobin 146, hematocrit 0.43 and platelet count 219. An ECG Holter monitor showed constant sinus rhythm of average frequency 67/min with night minimum of 45/min and daily maximum of 107/min. The total of 822 (0,9%) extra-systoles had been recorded, mostly ventricular extra-systoles with a single location stimulus, in the lower left ventricle wall. Sometimes short sequences of extra-systole bigeminy; 18 couplets (sometimes with bidirectional block); 56 interpolated extra-systoles and 1 short paroxysm (approx. 5 consecutive contractions) of short ventricular tachycardia of a 120/min frequency. Also, 22 atrial extra-systoles were noted. Reportedly, subjects symptoms subsided and did not recur afterwards. The subject was advised on low consumption of animal fat and salt and to continue Trombex (clopidogrel). The event transitory ischaemic attack was reported as resolving and the subject was discharged on 01/Feb/one year after*. At discharge the subject was afebrile and in a state of cardiopulmonary compensation. The investigator reported that there was not a reasonable possibility that the event transitory ischaemic attack was related to the blinded investigational product.

ADDITIONAL INFORMATION RECEIVED ON 20/FEB/one year after*: The event transitory ischaemic attack was reported as resolved on 01/Feb/one year after*. The symptoms did not recurr.

ADDITIONAL INFORMATION RECEIVED ON 28/FEB/one year after*: Discharge date was updated to 02/Feb/one year after*. Causality between the event transitory ischaemic attack and blinded investigational product was updated to Yes by the investigator.

ADDITIONAL INFORMATION RECEIVED ON 13/MAR/one year after*: The hospital discharge date was changed from 02/Feb/one year after*, back to the initially reported date of 01/Feb/one year after*. This date also corresponds to the hospital discharge summary report previously provided by the investigator.

Product : AMG 145 vs placebo Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

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SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
pain in right hip	Arthralgia (Pain in hip)	08-NOV-same year*---

Case Narrative : This 63 year old white female subject was participating in a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and experienced pain in right hip.

The subject's medical history provided by the investigator included hypercholesterolemia since eight years ago*. According to the investigator, the subject did not have previous episodes of pain in right hip. Previous treatment for the condition under study included simvastatin and Zarator (atorvastatin). The subject was not receiving any relevant concomitant medications at the time of the event.

The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 02/Nov/[redacted]. Approximately seven days later, on 09/Nov/same year*, the subject experienced pain in right hip and was hospitalized on that same date. Laboratory or diagnostic tests were not performed around the time of the event. Treatment medications included Pamol (paracetamol) and Contalgin (morphine sulfate). No further details were provided at the time of this report. The event was reported as resolved on 14/Nov/same year* and the subject was discharged from the hospital on the same day, without a final diagnosis. The subjects last dose of blinded investigational product prior to the event was on 02/Nov/same year*. Blinded investigational product was continued.

The investigator reported that there was no reasonable possibility that the event pain in right hip was related to the blinded investigational drug.

ADDITIONAL INFORMATION RECEIVED ON 28/FEB/one year after*: The events details were updated. The subject developed pain in the right hip on 08/Nov/same year*. The following day, on 09/Nov/same year* the subject was hospitalized for further evaluation and treatment. The subject was discharged from the hospital on 14/Nov/same year*. The event was reported to have resolved on 15/Dec/same year*.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	UNK	---	---	03-JAN-one year after*

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
worsening of spondylololistese	Spondylolisthesis (Spondylolisthesis)	23-JAN-one year after* (20 days)

Case Narrative : This 65 year old Caucasian female subject was participating in a clinical trial, a phase 2, randomized, double-blind, placebo and active controlled, dose-ranging, multiple-dose, parallel-group study to evaluate the LDL-C lowering properties of AMG 145, compared to placebo and ezetimibe when used as add-on therapy in dyslipidemic and developed spondylololistese.

The subject's medical history included hypercholesterolemia and spondylolisthesis since five years ago*. The previous treatment for the condition under study and concomitant medications were not provided by the investigator at the time of this report.

The subject received the first dose of blinded investigational study drug AMG 145 vs placebo on 08/Nov/[redacted]. Approximately one month and two weeks later, on 23/Jan/one year after*, the subject was admitted to the hospital to undergo spondylolisthesis surgery on the same day. The investigator stated that the subject underwent the surgery without complications. Treatment also included Zinaly (cetirizine hydrochloride). The event was reported as resolved on 25/Jan/one year after*; and the subject was discharged from the hospital on the same day. The subject's last dose of the blinded investigational product prior to the event was on 03/Jan/one year after*.

The investigator reported that there was a not reasonable possibility that the event spondylololistese was related to the blinded investigational drug.

ADDITIONAL INFORMATION RECEIVED ON 07/FEB/one year after*: Zinaly (cetirizine hydrochloride) was changed for Zinacef (cefuroxime). The investigator reported that no further information were available.

ADDITIONAL INFORMATION RECEIVED ON 16/FEB/one year after*: The investigator reported that the final diagnosis was worsening of spondylololistese. Additional medical history included hypertension and tremor left hand. Previous and ongoing treatment for the condition under study included simvastatin. Concomitant medications included Centyl plus potassium chloride (bendroflumethiazide, potassium chloride), amlodipine, propranolol and paracetamol. Additional treatment for the event included Vilan (nicomorphine), Perilax (bisacodyl) and Magnesia (magnesium hydroxide). The investigator reported that subject completed blinded investigational product on 03/Jan/one year after*.

The investigator reported that there was not a reasonable possibility that the event worsening spondylololistese was related to blinded investigational product.

Product : AMG 145 vs placebo Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	UNK	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Bladder cancer	Bladder cancer (Bladder cancer)	19-DEC-same year*---

Case Narrative : This 69 year old Caucasian male was participating in a phase 2, randomized, double-blind, placebo and active controlled, dose-ranging, multiple-dose, parallel-group study to evaluate the LDL-C lowering properties of AMG 145, compared to placebo and ezetimibe when used as add-on therapy in dyslipidemic and developed bladder cancer.

The subject's medical history included hypercholesterolemia and bladder cancer (6-7 years ago). Previous treatment for the condition under study and

concomitant medications were not reported by the investigator at the time of this report.

The subject received the first dose of blinded investigational study drug vs placebo on 22/Nov/[redacted]. Approximately 27 days later, on 19/Dec/same year*, at the yearly screening, recurrence of bladder cancer was noted. Subject was and is asymptomatic. The subject was started on therapy with Bacillus Calmette-Guerin via bladder irrigation. The investigator reported that thet subject could remain in study and continued study drug. The event was reported as resolving. Blinded investigational product was continued.

The investigator reported that there was a not reasonable possibility that the event bladder cancer was related to blinded investigational product.

Product : AMG 145 vs placebo Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	02-FEB-one year after*

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Angina aggravated	Angina pectoris (Angina pectoris aggravated)	27-FEB-one year after* (25 days)

Case Narrative : This 45 year old Caucasian male was participating in a phase 2, randomized, double-blind, placebo and active controlled, dose-ranging, multiple-dose, parallel-group study to evaluate the LDL-C lowering properties of AMG 145, compared to placebo and ezetimibe when used as add-on therapy in dyslipidemic and developed worsening of angina.

The subjects medical history included hypercholesterolemia, aggressive coronary artery disease, angina, history of multiple angioplasty and stenting, coronary artery bypass graft, chronic smoker, hypertension, and occasional alcohol use. The subject had family history of coronary artery disease in a brother. Previous treatment for the condition under study was not provided by the investigator at the time of this report. Concomitant medications included diltiazem, Aspirin (acetylsalicylic acid) and Crestor (rosuvastatin calcium).

The subject received the first dose of blinded investigational study product on 21/Nov/[redacted]. On 01/Jan/one year after*, the subject complained of worsening of angina (which was captured as adverse event). Approximately three months after initiation of first dose, on 27/Feb/one year after*, the subject presented to the hospital with left side intermittent chest pain, which radiated to the left jaw and was associated with mild shortness of breath. He had been taking nitroglycerin without relief. The subject was hospitalized on the same day. His vital signs included blood pressure 165/94, respiratory rate 16, oxygen saturation 98% and body temperature 96.5. An electrocardiogram showed multiple PVCs and sinus rhythm. The following day, on 28/Feb/one year after*, the subject underwent coronary angiography which revealed engagement of the left main did not show dampening of pressures. The left main was diffusely diseased. The circumflex was diffusely diseased with an 80-90% proximal lesion and eventually another 80% lesion, but this was after giving rise to an arterial branch that was an atrial branch that was giving collaterals to the distal right coronary artery. The rest of the obtuse marginal was completely occluded. The LAD was completely occluded at its proximal portion. Engagement of the right coronary was done without dampening of pressures. The right was 100% occluded at its mid portion. A left ventriculogram revealed left ventricular end diastolic pressure measured approximately 10. Ejection fraction by visual

estimation appeared to be in the order of 60%. There was no gradient across the aortic valve and no evidence of mitral regurgitation noted. Central aortic pressure was about 118 with an LV pressure about 118. A reverse saphenous vein graft injection revealed engagement of the saphenous vein graft to the right coronary artery demonstrating a 95% lesion with TIMI grade 2 flow and eventually demonstrating this was the culprit vessel. Reverse saphenous vein graft injection to the obtuse marginal showed a widely patent channel with some areas of disease. The entire conduit was free of significant stenosis. The touchdown site was excellent and brisk antegrade and retrograde filling was noted. A reverse saphenous vein graft injection to the second obtuse marginal revealed a 100% occlusion at its proximal portion. A LIMA graft injection demonstrated a widely patent conduit with no evidence of disease throughout its course. The touchdown site was excellent without evidence of significant problems. The subject underwent successful balloon angioplasty and stenting to the saphenous vein graft. During the procedure, non-Q-wave myocardial infarction was also revealed. Laboratory test showed ranging values as follows: creatine phosphokinase from 76 to 118, creatine phosphokinase MB from <0.5 to 1.0 and troponin from 0.25 to 0.99. Additional treatment included nitroglycerin. The event was reported as resolving at the time of this report and the subject remained hospitalized. The last dose of blinded investigational product prior to the event was on 02/Feb/one year after*. The investigator reported that the subject completed the study on 27/Feb/one year after*.

The investigator reported that there was no reasonable possibility that the event worsening of angina was related to the blinded investigational product.

ADDITIONAL INFORMATION RECEIVED ON 20/MAR/one year after*: Additional concomitant medications included Plavix (clopidogrel bisulfate). The subject underwent cardiac catheterization with a complex balloon angioplasty and stenting of the saphenous vein graft to the right coronary artery with a 5 x 15 mm Multi-Link Cobalt Vision stent with less than 15% residual stenosis. Reportedly, after the procedure, his right groin was slightly tender, therefore on 29/Feb/one year after*, a femoral artery ultrasound was performed. There was no evidence of a pseudoaneurysm. The subjects Plavix dosage was stopped and he was started on Effient (prasugrel hydrochloride). The event was reported as resolved on 29/Feb/one year after*, and the subject was discharged from the hospital on 01/Mar/one year after*.

ADDITIONAL INFORMATION RECEIVED ON 13/APR/one year after*: Previous treatment for the condition under study included simvastatin. On 27/Feb/one year after*, electrocardiogram showed sinus rhythm, borderline prolonged QT interval, baseline wander in lead (s) V1 and heart rate of 96. On 29/Feb/one year after*, electrocardiogram showed sinus rhythm and heart rate of 77. On 01/Mar/one year after*, repeat electrocardiogram showed sinus rhythm, heart rate of 75 and anteroseptal infarct was considered. Date when laboratory tests were carried out was updated to 27/Feb/one year after*.

ADDITIONAL INFORMATION RECEIVED ON 27/APR/one year after*: The event of worsening of angina was updated to angina aggravated.

Product : AMG 145 vs placebo Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	28-OCT-same year*

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Penile bleeding	Penile haemorrhage (Penile hemorrhage)	05-NOV-same year* (8 days)

Case Narrative : This 65 year old Caucasian male subject was participating in a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-COA reductase inhibitors in hypercholesterolemic subjects and developed bladder tumor and penile bleeding.

The subjects medical history provided by the investigator included hypercholesterolemia, urinary tract infection, urinary urgency and frequency, hematuria, back pain and kidneys separation. Previous treatment for the condition under study was not provided by the investigator at the time of this report. Concomitant medications included Crestor (rosuvastatin calcium), Ambien (zolpidem tartrate), Flexeril (cyclobenzaprine hydrochloride) and omeprazole.

The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 28/Oct/[redacted]. The investigator stated that the subject did not report any serious adverse event or new conmeds. However according to the medical records a week earlier, on 21/Oct/same year*, the subject presented to the emergency room due to lower back pain and hematuria. A computerized tomograph (CT) was done showing a mass associated with the anterior bladder wall extending mostly into the fat anterior to the bladder; this could represent bladder tumor or urachal remnant tumor; adenopathy in the right common iliac chain; soft tissue nodule against the left hemidiaphragm above the kidney (new and suspicious for tumor nodule); an inferior right liver lesion; could not exclude metastatic disease (this did not appear on prior study). The subject was diagnosed with a bladder mass, enlarged right iliac lymph node, nodule near the crus of the left hemi diaphragm and liver lesion. On 24/Oct/same year*, the subject was seen by an urologist, and ten days later, on 04/Nov/same year*, a cystoscopy/bilateral retrograde pyelogram was performed revealing lobular appearing mass involving the bladder dome near the region of the urachus; there were areas on this consistent with necrosis; this was concerning for urachal adenocarcinoma. Bilateral retrograde pyelogram demonstrated no areas of filling defect on dynamic imaging; it appeared that there was reasonable filling of the collecting system bilaterally; prompt drainage. That day, the subject underwent Foley catheter placement and was discharged from the hospital. The next day, 05/Nov/same year*, the subject was seen twice in the emergency room due to Foley catheter displacement; and later that day was admitted to the hospital to avoid any additional trauma on his penis. The subject was diagnosed with metastatic bladder cancer, stage IV. Two days later, on 07/Nov/same year*, the subject was discharged from the hospital. The subject missed his visit 3 appointment on 08/Nov/same year*; and until a week later, on 15/Nov/same year*, was contacted via phone call. The subject was upset and reported that he had been in the hospital and was diagnosed with bladder cancer. On 17/Nov/same year*, a CT of chest performed showed the trachea and mainstem bronchi were patent; the lungs were clear; calcified subcarinal and left hilar nodes of old granulomatous disease; no adenopathy, normal heart size; no pleural or pericardial effusion; upper abdomen remarkable for splenic granulomata and left nephrectomy; no evidence for metastatic disease. Also a nuclear magnetic resonance of the bone was done revealing non-specific focal increased radiotracer uptake of the right inferior scapula; this raised the possibility for metastatic disease although no definite lesion was present on the subject's CT scan. There were multiple areas of apparent joint uptake likely degenerative in nature. The outcome of bladder tumor was not provided; the outcome of penile bleeding was reported as not resolved. Blinded investigational product was permanently discontinued, as the subject no longer wished to participate in the study. The subject was asked to consider to complete his study visits without study medication; however further contact with the subject had been unsuccessful.

The investigator reported that there was no reasonable possibility that the event bladder tumor and penile bleeding were related to the blinded investigational product.

ADDITIONAL INFORMATION RECEIVED ON 31/JAN/one year after*: After the investigator reviewed the subjects medical record, he considered the bladder tumor as not serious and this event was deleted, retaining the penile bleeding event.

ADDITIONAL INFORMATION RECEIVED ON 14/FEB/one year after*: The subject's medical history included right liver lesion, adenopathy of right common iliac

chain, tumor nodule (left hemidiaphragm) and history of bladder mass. On 04/Nov/same year*, cystoscopy showed normal appearing anterior urethra and slightly enlarged prostate. Bilateral orthotopic ureteral orifices were seen in the bladder. There was a lobular-appearing tumor involving anterior bladder wall. Maximum diameter was between 1 and 2 cm. There were areas on this that appeared to be concerning for necrosis. Biopsy of the posterior bladder wall was carried to rule out occult malignancy. Rectal examination demonstrated that bladder did not appear fixed.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
COPD exacerbation	Chronic obstructive pulmonary disease (COPD exacerbation)	25-SEP-same year*---
Syncope	Syncope (Syncope)	25-SEP-same year*---
UTI	Urinary tract infection (UTI)	25-SEP-same year*---

Case Narrative : This 55 year old female subject was participating in a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and experienced syncope, urinary tract infection (UTI) and chronic obstructive pulmonary disease (COPD) exacerbation.

The subjects medical history included hypercholesterolemia, chronic urinary tract infection, uncontrolled type II diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease with multiple episodes of exacerbated bronchitis, asthma, vertigo, gastroesophageal reflux disease, hypertension, neuropathy secondary to diabetes mellitus, bipolar disorder, chronic tobacco use since she was 16 years old, osteoarthritis, degenerative joint disease, morbid obesity with a BMI over 40, congestive heart failure, three ectopic pregnancies, hysterectomy, "IBS" (irritable bowel syndrome), depression, anxiety, and allergy to opioids and codeine. Previous treatment for the condition under study was not provided by the investigator at the time of this report. Concomitant medications included clopidogrel, metformin, simvastatin, ranitidine, lorazepam, furosemide, topiramate, meloxicam, hydroxyzine, iloperidone and Elavil (amitriptyline hydrochloride).

The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 29/Aug/[redacted]. Approximately one month later, on 25/Sep/same year*, the subject presented to the Emergency Room (ER) concerned about syncope. The subject was hypoxic, pushed herself to continue going to the bathroom, and subsequently fell in her kitchen. She stated, "I just slowly went down." The subject's husband found her and brought her to the ER immediately. There were no injuries associated with the fall, however she complained of a headache where she hit her head during the fall. The subject denied chest pain or other pain or discomfort but complained of a tired feeling. She was awake, alert and oriented. The subject indicated that she had not been taking her nebulizer treatments and she had an exacerbation of bronchitis with a recent increase in coughing over the past few days. Upon arrival, her vital signs revealed that her temperature was 97.5 degrees Fahrenheit, blood pressure (BP) was 100/55, pulse was 101, respirations were 20 and oxygen saturation was 94 %. Approximately fifteen minutes later, her BP was 103/48, pulse was 98, respirations were 20 and oxygen saturation

remained at 94 %. Five minutes later, her BP was 91/55. She was placed on oxygen, 2 L per nasal cannula. Physical examination revealed tenderness in the back, at lungs, multiple wheezes, both loose and tight bilateral lobes, she moved air and had an occasional loose rhonchi. Wheezes on both inspiration and expiration were also noted, however, these were not tight. It was determined that this was more excessive than her baseline. Additionally, chronic trace edema bilaterally on extremities was noted. Chest X-ray and computerized tomography of the head were negative. An electrocardiogram revealed sinus rhythm with first degree block, normal P axis, V rate of 50-99, prolonged PR interval of >205, V rate of 91-120, left atrial enlargement of P'>60 ms >-0.15 MV V1, borderline T abnormalities and diffuse leads. Urine culture microbiology showed >100 000 colonies /mL Gram negative rods. The subject was diagnosed with asymptomatic UTI and COPD exacerbation. The subject was started on ipratropium and Albuterol (salbutamol). The subject's pulse rate ranged from 87 - 102, respirations ranged between 18 - 20, blood pressure ranged from 92/74 - 140/85, blood glucose was 110 and her oxygen saturation fluctuated between 94 % and 98 %. Elavil was withheld and outpatient medications were restarted in addition to Rocephin (ceftriaxone). The subject had no further bouts of dizziness and she wanted to go home. The event syncope was reported to have resolved on 25/Sep/same year* and the subject was discharged from the hospital the following day, on 26/Sep/same year*, with her regular outpatient medications plus Cipro (ciprofloxacin), Medrol Dosepak (methylprednisolone), Mucinex (guaifenasin) and DuoNeb (ipratonium bromide, salbutamol sulfate). The event COPD exacerbation was reported to have resolved on 02/Oct/same year*. The subject continued her antibiotic treatment until 06/Oct/same year* therefore the event UTI was reported to have resolved. The subject's last dose of blinded investigational product prior to the event was on 12/Sep/same year*. Blinded investigational product was continued.

The investigator reported that there was no reasonable possibility that the events syncope, UTI and COPD exacerbation were related to the blinded investigational product.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Acute decompensation of systolic congestive heart failure	Cardiac failure acute (Acute decompensated heart failure)	08-OCT-same year*---

Case Narrative : This 59 year old white male subject was participating in a TIMI 57 - a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and developed acute decompensation of systolic congestive heart failure.

The subject's medical history included chronic hypercholesterolemia, hypertension, ex smoker, type II diabetes mellitus with vascular complications, coronary artery disease, coronary artery bypass graft, congestive heart failure (CHF), ejection fraction of 35 % (February same year*), endogenous obesity, herpes zoster on the left scalp, neuropathy, cardiomyopathy, cerebrovascular accident, transient ischemic attack, carotid artery occlusion, hypokalemia, depression, renal insufficiency, bilaterally cataract extractions, ex-smoker, cardiac catheterization after presenting with an anginal syndrome and abnormal stress test, triple vessel disease, distal disease as well as non-revascularizable diagonal disease, and left carotid occlusion with a cerebellar infarct. Subjects non compliance with medication was also mentioned. Previous treatment for the condition under study was not provided by the investigator at the

time of this report. According to the Concomitant medications included Flovent HFA (fluticasone propionate), furosemide, potassium chloride, Coreg (carvedilol), hydralazine hydrochloride, Norvasc (amlodipine), lisinopril, Aspirin (acetylsalicylic acid), Lexapro (escitalopram oxalate), Lipitor (atorvastatin calcium), nitroglycerin, Wellbutrin (bupropion hydrochloride), clonidine hydrochloride, Levemir (insulin), NovoLog (insulin aspartate), Plavix (clopidogrel), Pepcid (famotidine), Lortab(hydrocodone/acetaminophen), oxygen and bupropion.

The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 14/Sep/[redacted]. Approximately one month later, on 08/Oct/same year* the subject was seen in the morning by his primary care provider and he felt fine. In the afternoon, the subject started to feel some chest discomfort with a brief episode of left arm tingling and numbness and shaking in his legs which resolved spontaneously. The subject ate a normal dinner, he went to lie down for bed and he started to feel worsening chest discomfort and shortness of breath. He also started to cough up clear sputum, and he began to feel dizzy like he was going to lose consciousness. The subject called the ambulance to bring him to the Emergency Department. The subject denied chest pain, palpitations, pleuritic pain, nausea, vomiting, diarrhea, abdominal pain, dysuria or recent leg swelling. In the ambulance, the subject received sublingual nitroglycerin, intravenous Lasix (furosemide), oxygen and albuterol nebulizer. Upon arrival, his symptoms had resolved. In the Emergency Department, the subject was given enalapril and nitroglycerin paste with continued oxygen therapy. The subject was admitted to the hospital on the same day with acute decompensation of systolic congestive heart failure diagnosis. The investigator stated that shortness of breath was likely caused by flash pulmonary edema caused by underlying CHF. During the course of hospitalization, the subject's hypertension remained stable. Ischemia was reported as the cause of congestive heart failure. The subject's initial troponin value was 0.05 that come back to 0.09 and 0.10, which were borderline elevated in the setting of a creatinine of 1.3. Upon admission, his vital signs were pulse rate of 79, respiratory rate of 22, blood pressure of 126/61, oxygen saturation of 94 % on three liters of nasal cannula and body temperature of 37.2. Chest X-ray showed diffuse interstitial prominence impression, worsening congestive heart failure and bilateral interstitial edema with cardiomegaly. Laboratory data disclosed white blood cell (WBC) count of 18.1, plasma of 308 mg/dl, neutrophil percentage 68 %, hemoglobin of 18.3, hematocrit of 52.3 %, platelet count of 240, sodium of 144, potassium of 4.2, chloride of 105 and blood urea nitrogen of 24. On 09/Oct/same year*, repeated laboratory data disclosed troponin of 0.07 ng/mL, WBC count of 9.6 Tho/uL, red blood cell count of 4.88 Mil/uL, hemoglobin of 14.7 g/dL, hematocrit of 43 %, platelet count of 165 Tho/uL, creatinine of 1.6 mg/dL, estimated glomerular filtration rate of 44 mL/min, sodium of 144 mEq/L, potassium of 3.2 mEq/L and chloride of 105 mEq/L. An echocardiogram showed diastolic dysfunction and LVEF of 50 % to 55 %. No signs of an acute myocardial infarction. Septal wall motion abnormality that was secondary to left bundle branch block. Mild left ventricular dysfunction, aortic sclerosis and mild insufficiency of mitral and tricuspid valve, mild and flow pattern suggested restricted filling pattern. The subject was stable during hospitalization and did not complain of any palpitations. Additional treatment medication included Lovenox (enoxaparin sodium). The event was reported to have resolved on 09/Oct/same year* and the subject was discharged from the hospital on the same day with stable condition. The subject was advised on low cholesterol, low fat and low salt diabetic diet. The subjects last dose of investigational product prior to the event was on 28/Sep/same year*. No action was taken with study medication.

The investigator reported that there was no reasonable possibility that the event acute decompensation of systolic congestive heart failure was related to the blinded investigational drug.

Product : AMG 145 vs placebo Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

List of Safety Narratives - Main Page

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Atypical angina	Angina pectoris (Atypical angina)	15-NOV-same year*---

Case Narrative : This 50 year old white male subject was participating in a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and developed atypical angina.

The subject's medical history provided by the investigator included hypercholesterolemia, arteriosclerotic heart disease with previous drug-eluting stents to the left anterior descending, obtuse marginal and posterior descending artery, normal left ventricular function, hypertension, cardiac catheterization, tonsillectomy, four hernia repairs, right anterior knee cruciate ligament repair and non-smoker. The subject had family history of multiple sclerosis and arteriosclerotic heart disease. Previous treatment for the condition under study and ongoing medication included Crestor (rosuvastatin calcium). Concomitant medications included Effient (prasugrel hydrochloride), Asa (acetylsalicylic acid), Imdur (isosorbide mononitrate), Altace (ramipril), Coreg (carvedilol), Cipro (ciprofloxacin) and Flagyl (metronidazole).

The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 13/Sep/[redacted]. Approximately two months later, on 15/Nov/same year*, the subject presented to the hospital for his scheduled dose of blinded investigational product and a routine blood test and had a significant increase of nausea with some associated sweats. Afterwards, he went to work and began to develop chest discomfort, intermittent palpitations, substernal pain, intermittent stabbing and constant pressure. Chest discomfort was described as left pectoral portion the chest with radiation into his neck. The episode lasted about 30 minutes and occurred at rest. He took two shots of nitroglycerin (glyceryl trinitrate) and had prompt relief of the discomfort. However the pain came back for which reason he went to the emergency room and was admitted. His vital signs were blood pressure of 104/73, pulse of 54, temperature of 98.1, respiratory rate of 14, oxygen saturation at room air of 98 and had a pain score of 2. Reportedly, the subject had recently been diagnosed with colitis via computed tomography of the abdomen and a flexible sigmoidoscopy. Laboratory tests revealed white blood cell count of 7.7, hemoglobin of 14.1, hematocrit of 40.5, platelet count of 163,000, international normalization ratio of 1.1, D-dimer less than 0.23, sodium of 137, potassium of 4, chloride of 102, glucose of 130, urea of 9, creatinine of 1.07, calcium of 89, glomerular filtration rate of 73.2, creatinine clearance of 94. Cardiac enzymes were negative. The subject was diagnosed with atypical angina without evidence of acute coronary ischemia. The following day, on 16/Nov/same year*, the subject underwent cardiac catheterization with catheter insertion and exchange, percutaneous transluminal coronary angioplasty wire insertion, stent insertion and balloon insertion. Surgery and postsurgical period were uncomplicated. Laboratory tests revealed creatinine of 1.12, glomerular filtration rate of 69.4, international normalization ratio of 1.1, prothrombin time of 14.2 sec and white blood cell count of 7.5. A chest x-ray showed normal chest; unremarkable and a twelve lead electrocardiogram revealed sinus bradycardia with no acute ischemic changes. Further treatment medication included Versed (midazolam hydrochloride), fentanyl, Zofran (ondansetron), Angiomax (bivalirudin), normal saline (sodium chloride) and lidocaine. The event atypical angina was reported as resolved on 16/Nov/same year*, and the subject was discharged on that same date. The subject's last dose of blinded investigational product was on 15/Nov/same year*. Blinded investigational product was continued.

The investigator reported that there was no reasonable possibility that the event atypical angina was related to the blinded investigational product.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

List of Safety Narratives - Main Page

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
Worsening of coronary artery disease	Coronary artery disease (Coronary artery disease aggravated)	14-OCT-same year*---

Case Narrative : This 61 year old Caucasian male subject was participating in a clinical trial, LAPLACE TIMI 57 - a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and developed worsening of coronary artery disease.

The subject's current medical condition provided by the investigator included hypercholesterolemia (controlled by medications), dyspnea on exertion, angina, type 2 diabetes mellitus, alcohol use (moderate), hypertension, non-smoker, atherosclerotic coronary artery disease, hernia repair, cardiac catheterization, tonsillectomy, clavicle repair and drug allergy to Avandia (rosiglitazone) and Altace (ramipril). Previous and current treatment for the condition under study included simvastatin and fish oil. Concomitant medications included lisinopril, glipizide, metformin, multivitamins, ASA (acetylsalicylic acid), "saw palmetto", "glypinamid", Cinnamon (Cinnamomum verum), Coreg (carvedilol), Imdur (isosorbide mononitrate) and Sinemet (carbidopa/levodopa).

Prior to the first dose of the blinded investigational product, on 07/Sep/same year*, the subject underwent cardiac catheterization that revealed multivessel atherosclerotic heart disease. The subject was started on carvedilol and Imdur. The investigator stated that the subject would need a bypass surgery; however the subject wanted to delay the surgery until retirement (at age of 63). The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 19/Sep/[redacted]. Approximately two weeks later, on 04/Oct/same year*, the subject presented to a follow up visit after left heart catheterization. Anginal symptoms included shortness of breath when the subject was lifting his arms above the level of his shoulders. The subject stated that he had noticed some improvement in his symptoms after being started on Imdur and Coreg. Physical examination showed extremities without edema, clubbing, cyanosis, or calf tenderness; peripheral pulses were intact, and cardiac examination showed no murmurs, gallops, no lift, heave or thrill. He stated that he was almost able to cut his entire lawn without stopping. Imdur dose was increased from 30 mg to 60 mg per day. Ten days later, on 14/Oct/same year*, the subject experienced worsening of coronary artery disease. He was seen in follow up visit. He reported easy fatigability and vague chest discomfort; and stated that he would undergo the bypass surgery. Vital signs were blood pressure of 132/82, heart rate of 56; physical examination showed extremities without edema and no cardiac murmurs or gallops. Almost one month later, on 11/Nov/same year*, the subject presented to the hospital to undergo coronary artery bypass grafting. Physical examination revealed cardiac regular rhythm without murmur and good perfusion in all four extremities. Cardiac catheterizations were reviewed, and the subject had slightly reduced ejection fraction (EF) with anterior wall that was mildly hypokinetic; EF of 55 %. Pulmonary pressures were essentially normal. The left anterior descending artery had a proximal 50% stenosis and then this was followed by a 90% stenosis that involved diagonal artery. The circumflex system was essentially free of significant disease and probably would not need any grafting. The right coronary artery distally at the take off of the posterior descending artery had a high grade of stenosis and it was anticipated that the subject would need grafting to the posterior descending artery. That day, the subject underwent coronary artery bypass grafting x3, consisting of left internal mammary artery to the left descending artery, aorto-saphenous vein graft to the diagonal artery, aorto-saphenous vein graft to the posterior descending artery. The subject underwent the procedure without complications and was transferred to the Cardiovascular Surgical Intensive Care Unit in stable condition. The event was reported to have resolved on 11/Nov/same year*. Relevant laboratory test results from 11/Nov/same year* to 16/Nov/same year*, showed magnesium level ranged from 2.3

mg/dL to 2.1 mg/dL; total protein of 3.9 g/dL, sodium level ranged from 138 mEq/L to 133 mEq/L, potassium from 3.8 mEq/L to 3.6 mEq/L, random glucose from 186 to 108 mg/dL, calcium from 7.3 to 8.4 mg/dL and hemoglobin ranged from 12.4 g/dL to 10.4 g/dL. The subject was discharged from the hospital on 16/Nov/same year*. The subject's last dose of the blinded investigational product prior to the event was on 10/Nov//same year*. The blinded investigational product was continued.

The investigator reported that there was no reasonable possibility that the event worsening of coronary artery disease was related to the blinded investigational product.

ADDITIONAL INFORMATION RECEIVED ON 19/JAN/one year after*: The investigator confirmed the onset and the end date of the event worsening of coronary artery disease as 14/Oct/same year* and 11/Nov/same year* respectively.

Product : AMG 145 vs placebo

Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
pulmonary emboli	Pulmonary embolism (Pulmonary embolism)	30-SEP-same year*---

Case Narrative : This 72 year old Caucasian male subject was participating in a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and developed pulmonary emboli.

The subjects medical history included hypercholesterolemia, type 2 diabetes mellitus, history of myocardial infarction, hypertension, disease of magnesium metabolism, sleep apnea, coronary atherosclerosis, aortocoronary bypass, rotator cuff surgery, cardiac catheterization, gout, erectile dysfunction, coronary artery disease and depression. The investigator reported that the subject had received previous treatment for the condition under study. Concomitant medications included Corgard (nadolol), Glucophage (metformin hydrochloride), Altace (ramipril),Allopurinol (allopurinol), Viagra (sildenafil citrate), Asa (acetylsalicylic acid), Glipizide (glipizide), metformin hydrochloride, Multivitamin (ascorbic acid, calcium pantothenate, ergocalciferol, nicotinamide, pyridoxine hydrochloride, retinol, riboflavin, thiamine hydrochloride), Vitamin C (ascorbic acid), Vitamin B12 (cyanocobalamin), Lexapro (escitalopram oxalate), Abilify (aripiprazole), Lipitor (atorvastatin calcium), Triplex (trifluoperazine hydrochloride), Welchol (colesevelam hydrochloride) and Celebrex (celecoxib).

On 13/Sep/same year*, the subject underwent rotator cuff surgery. The subject received the first dose of blinded investigational product AMG 145 vs placebo for hypercholesterolemia on 23/Sep/[redacted]. Approximately seven days later, on 30/Sep/same year*, the subject presented to the hospital with one day history of increasing shortness of breath. The subject underwent pulmonary function test which did not show any difference from previous test. An x-ray showed no infiltrate or pleural effusion. A computerized axial tomography of the chest revealed right pulmonary embolus and the subject was admitted to the hospital

on the same day. His vital signs were saturation rate of 98%, blood pressure of 130/70, respiratory rate of 20 and body temperature of 97.8. A physical examination revealed breath sounds were diminished bilaterally, with prolonged expirations and there were bilateral fine crepitations, otherwise his physical examination was grossly within normal limits. Laboratory tests revealed activated partial thromboplastin time (aPPT) of 24.6 secs, magnesium of 2.0 mg/dl, potassium of 5.2 mmol/l, urea of 22 mg/dl, hematocrit of 46.8%, hemoglobin of 14.9 g/dL, international normalized ratio (INR) of 1.15, prothrombin time (PT) of 11.8 secs, platelet count of 267x10^3/uL, red blood cell count of 4.93x10^6/uL and white blood cell count of 9.8x10^3/uL. A Blood gasometry showed pH of 7.4, partial pressure of carbon dioxide (pCO2) of 42 mmHg, partial pressure of oxygen (PO2) of 70 mmHg, bicarbonate (HCO3) of 25.4 mEq/L, saturation of 94% and base excess of 1.4 mEq/L. A urinalysis revealed clear, yellow, ph 5.5 urine with specific gravity of 1.010; protein, glucose, blood, nitrite, bilirubin and leukocyte esterase negative, trace of ketones and urobilinogen of 0.2mg/dl. On a sputum culture no methicillin-resistant Staphylococcus aureus were detected. An echocardiogram revealed an ejection fraction of approximately 50-55%, low-normal LV systolic function. Additionally, there was moderate concentric left ventricular hypertrophy as well as mild mitral regurgitation. The subject was started on Coumadin (warfarin sodium) and Lovenox (enoxaparin sodium). The event was reported as resolved on 06/Oct/same year* and the subject was discharge on that same date. Upon discharge, laboratory tests revealed aPPT of 64.2 secs, potassium of 4.2mmol/l, urea of 16mg/dl, hematocrit of 41.5%, hemoglobin of 13.3g/dL, INR of 1.78, PT of 18.1 secs and white blood cell count of 7.0x10^3/uL. According to the hospital discharge summary the patient had pulmonary emboli secondary to being in bed. The subject had recent shoulder surgery, cardiac bypass, rotator cuff surgery on 13/Sep/same year* and history of cardiac catheterization 8 weeks ago. The last dose of the blinded investigational product prior to the event was on 23/Sep/same year*. The blinded investigational product was continued.

The investigator reported that there was no reasonable possibility that the event pulmonary emboli was related to the blinded investigational product. There were no co-suspected medications as reported by the investigator.

Product : AMG 145 vs placebo Study Drug Administred : Yes

Case Number	Study ID	Patient ID	Center ID	Related Case	Death Case	Death Date	Dose	Patient Route of Administration	Frequency	Last Dose
[redacted]	20101155	[redacted]	[redacted]	No	No	---	---	---	---	---

SAE Reported Term	SAE Preferred Term (SAE Lower Level Term)	Onset Date (Time to Onset)
coronary artery bypass graft	Coronary artery bypass (Coronary artery bypass graft)	02-NOV-same year*---

Case Narrative : This 59 year old white female subject was participating in a double-blind, randomized, placebo-controlled, multicenter, dose-ranging study to evaluate tolerability and efficacy of AMG 145 on LDL-C in combination with HMG-CoA reductase inhibitors in hypercholesterolemic subjects and underwent a coronary artery bypass graft.

The subject's medical history provided by the investigator included hypercholesterolemia, coronary artery disease, diabetes mellitus, joint surgery, shoulder surgery, wrist surgery, hand surgery, hysterectomy, cholecystectomy, appendectomy and is a non-smoker. The subject had family history of coronary artery disease and diabetes. Previous treatment for the condition under study included lovastatin. Concomitant medications included Aspirin (acetylsalicylic acid), simvastatin and metoprolol.