aminotransferase increased. The investigator considered blood bilirubin increased, alanine aminotransferase increased, and aspartate aminotransferase increased serious and not related to the study drug but related to disease progression; peripheral edema serious and not related to the study drug.

On 22 Sep 2015 (Day 565, 49 days after the last dose), the subject died due to disease progression.

Subject Number	43011003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-013431
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Vomiting

A 58-year-old white male was diagnosed with hepatocellular carcinoma on 31 Aug 2014. Significant medical history included diabetes mellitus, diarrhea, hepatic steatosis, hepatitis B, hypertriglyceridemia, decreased vitamin D, upper abdominal pain, and asthenia. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included carvedilol, clobetasol, colecalciferol, entecavir, glibenclamide, granisetron, lactulose, lercanidipine, lidocaine, magnesium, metformin, other agents for treatment of hemorrhoids (aflumycin gentamicin sulfate, and prednisolone), other emollients and protectives (salik cream), oxycodone, procto-glyvenol, ramipril, simvastatin, sodium chloride, tramadol, and triamcinolone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at segment 6 and 7 of right liver lobe, left lobe, diffuse liver lesions, and porta-hepatis lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 18 Feb 2015 (Day 1), treatment with study drug was initiated.

On 05 Aug 2015 (Day 169), the subject experienced decreased weight (Grade 2) with body weight of 78.8 kg (Baseline: 97 kg). On 01 Oct 2015 (Day 226), the event worsened to Grade 3 with body weight 71.4 kg and the study drug dose was reduced to 8 mg/day due to this event. The subject did not recover from decreased weight. The Investigator considered decreased weight nonserious and possibly related to the study drug.

On 23 Dec 2015 (Day 309), the study drug was interrupted due to suspected disease progression. Laboratory tests showed albumin 30 g/L (NR: 35 – 55), ALP 583 U/L (NR: 43 – 115), ALT 202 U/L (NR: 10 – 40), AST 300 U/L (NR: 10 – 43), and GGT 780 U/L (NR: 10 – 49). On 29 Dec 2015 (Day 315), the subject was withdrawn from the study due to clinical disease progression and received the last dose of the study drug on 22 Dec 2015 (Day 308).

On 04 Jan 2016 (Day 321), tumor response assessment showed disease progression. On 06 Jan 2016 (Day 323), Child Pugh score was 9.

On 09 Jan 2016 (Day 326), the subject was hospitalized for vomiting (Grade 3). The subject was treated with sodium chloride, lactulose, granisetron, and oxycodone. During the hospital stay, the subject experienced mild ascites and underwent paracentesis draining about 2 L with no evidence of spontaneous bacterial peritonitis. On 17 Jan 2016 (Day 334), the subject was discharged from the hospital. The subject did not recover from vomiting. The Investigator considered vomiting serious and not related to the study drug but related to disease progression.

On 25 Jan 2016 (Day 342), the subject was hospitalized for general physical health deterioration (Grade 4). On 29 Jan 2016 (Day 346, 38 days after the last dose), the subject died due to the general physical health deterioration. Autopsy was not performed. The Investigator considered general physical health deterioration serious and not related to study drug but related to disease progression.

Subject Number	44051006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-004466
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Cellulitis, Tumour necrosis, Liver abscess, Tumour rupture
AE(s) Leading to Discontinuation	Tumour necrosis, Liver abscess, Tumour rupture

A 63-year-old Chinese male was diagnosed with hepatocellular carcinoma on 13 Nov 2013. Significant medical history included gastroesophageal reflux disease, acute gastritis, benign gastric neoplasm, cholecystectomy, cholecystitis, cholelithiasis, diabetes mellitus, hepatitis B, hypercholesterolemia, hypertension, hepatic fibrosis, and decreased appetite. Previous anticancer therapies included radiotherapy to porta-caval node and therapeutic laparoscopy on liver segment 5. Prior and concomitant medications included adefovir, amlodipine, ampicillin, augmentin, cefepime, celecoxib, cetaphil, chlorphenamine, ciprofloxacin, dextrose and sodium chloride injection, fenofibrate, fentanyl, furosemide, heparinoid, hypnotics and sedatives, insulin glargine, lactulose, loperamide, loratadine, magnesium carbonate, magnesium sulfate, metformin, metoclopramide, morphine, omeprazole, panadeine co, paracetamol, piperacillin/tazobactam, potassium phosphate monobasic, sennoside a+b, sodium chloride, sodium polystyrene sulfonate, and telmisartan. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver, periportal lymph node, and right lower lobe lung mass. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 29 Dec 2014 (Day 1), treatment with study drug was initiated.

On 22 Feb 2015 (Day 56), the subject was hospitalized for subcutaneous cellulitis on right hypochondrium (Grade 3). On 23 Feb 2015 (Day 57), laboratory tests showed Hgb 81 g/L (NR: 125 – 170), WBC 12.5 x10^9/L (NR: 3.7 – 11), and platelet count 560 x10^9/L (NR: 125 – 375). On 25 Feb 2015 (Day 59), the subject experienced pyrogenic liver abscess (Grade 3), HCC tumor rupture (Grade 3), tumor necrosis (Grade 3), and anemia (Grade 3). The study drug was withdrawn due to pyrogenic liver abscess and tumor necrosis. Computed tomography of the abdomen and pelvis showed necrosis of two dominant liver tumors in segment 4B and 6 and rupture of segment 6 through the peritoneum into the subcutaneous tissue of right hypochondrium. The subject underwent CT guided drainage of liver abscess and was also treated with multiple packed red blood cell transfusions, fentanyl, sodium chloride, piperacillin/tazobactam, paracetamol, morphine, cefepime, ampicillin, magnesium sulfate, potassium phosphate monobasic, sodium polystyrene sulfonate, chlorphenamine, and heparinoid. The study drug was withdrawn due to pyogenic liver abscess, tumor necrosis, and tumor rupture. Laboratory tests showed Hgb 79 g/L (NR: 140 – 180), absolute neutrophil count 16.23 x10^9/L (NR: 2.0 – 7.5), and platelet count 559 x10^9/L (NR: 140 – 440). On 25 Feb 2015 (Day 59), tumor response assessment was disease progression and the subject was withdrawn from study due to disease progression. The subject received the last dose of the study drug on 24 Feb 2015 (Day 58). Blood culture was positive for aerobic organisms and aerobic culture of liver abscess showed multiple organisms from the liver fluid on gram stain. On 05 Mar 2015 (Day 67), the subject experienced hypoalbuminemia (Grade 2) and dependent edema likely secondary to

hypoalbuminemia (Grade 1) with albumin 22 g/L (NR: 40 – 51). The subject was treated with multiple human albumin transfusion and furosemide. On 24 Mar 2015 (Day 86), the subject recovered from subcutaneous cellulitis, HCC tumor rupture, and pyrogenic liver abscess. The subject did not recover from anemia, tumor necrosis, hypoalbuminemia, and dependent edema. The Investigator considered subcutaneous cellulitis serious and not related to the study drug; pyrogenic liver abscess, tumor necrosis, and HCC tumor rupture serious and not related to the study drug but related to the disease progression; anemia, hypoalbuminemia, and dependent edema secondary to hypoalbuminemia nonserious and not related to the study drug.

On 31 Mar 2015 (Day 93, 35 days after the last dose), the subject died due to disease progression.

Subject Number	45011010
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-012696
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Oesophageal varices haemorrhage, Upper gastrointestinal haemorrhage

A 65-year-old Chinese male was diagnosed with hepatocellular carcinoma on 11 Apr 2007. Significant medical history included hepatitis B, hepatic cirrhosis, and gastroesophageal reflux disease. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included acetylcysteine, algitab, ambroxol, cefixime, ceftriaxone, ciprofloxacin, cough and cold preparations, dextromethorphan, diosmectite, diphenhydramine, entecavir, esomeprazole, fexofenadine, furosemide, human albumin, lansoprazole, loperamide, methylprednisolone, metoclopramide, metronidazole, neotracin, pantoprazole, paracetamol, potassium, proctosedyl, silybum marianum, spironolactone, strocain, terlipressin, tramadol, tranexamic acid, urea, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left liver lobe and right portal vein thrombosis. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 06 Jun 2014 (Day 1), treatment with study drug was initiated.

On 19 Jun 2014 (Day 14), the subject experienced fatigue (Grade 1). On 07 May 2015 (Day 336), the fatigue worsened to Grade 2 and the study drug was interrupted due to this event. On 21 May 2015 (Day 350), the severity of fatigue improved to Grade 1. The study drug was resumed at a reduced dose of 8 mg/day due to fatigue. The subject did not recover from fatigue. The Investigator considered fatigue nonserious and possibly related to the study drug.

On 04 Dec 2015 (Day 547), the subject was hospitalized for esophageal varices hemorrhage (Grade 3). On 07 Dec 2015 (Day 550), upper gastrointestinal tract endoscopy revealed esophageal varices and the subject underwent variceal ligation. Laboratory tests showed RBC 3.11 x10^12/L (NR: 4.1 – 5.55), Hgb 103 g/L (NR: 139 – 191), PT 16.3 sec (NR: 9.4 – 12.5), and INR 1.47 (NR: 0.8 – 1.2). The subject was treated with fresh frozen plasma transfusion, pantoprazole, ceftriaxone, and terlipressin. On 08 Dec 2015 (Day 551), the study drug was interrupted due to this event. On 11 Dec 2015 (Day 554), repeat laboratory test showed Hgb 87 g/L and the subject was discharged from the hospital. On 12 Dec 2015 (Day 555), the subject recovered from esophageal varices hemorrhage. On 13 Dec 2015 (Day 556), the study drug was resumed at same dose of 8 mg/day. The Investigator considered esophageal varices hemorrhage serious and not related to the study drug.

On 18 Dec 2015 (Day 561), the subject was hospitalized for upper gastrointestinal hemorrhage (Grade 3), confirmed by upper gastrointestinal tract endoscopy. The subject was treated with esomeprazole and terlipressin. The study drug dose did not change. On 22 Dec 2015 (Day 565), the subject recovered from upper gastrointestinal hemorrhage. The Investigator considered upper gastrointestinal hemorrhage serious and not related to the study drug.

The subject remained in the study at the time of data cut-off.

Subject Number	45021001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01421-CLI-TW
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Liver carcinoma ruptured, Metastases to spine
AE(s) Leading to Discontinuation	Liver carcinoma ruptured

A 56-year-old Chinese male was diagnosed with hepatocellular carcinoma on 07 Aug 2013. Significant medical history included abdominal pain, blurred vision, chronic obstructive pulmonary disease, debridement of epidural space, laryngoscopy, epiglottic cyst, gastric ulcer, hepatic steatosis, hepatitis C, hydronephrosis, hypertension, renal stone removal, left ureterolithiasis, hepatic cirrhosis, lower back pain, intervertebral disc operation, psoriasis, medical device removal (spinal implant removal), medical device implantation (syntec implant), spinal laminectomy (L2 – L3), spinal osteoarthritis, subcutaneous panniculitis, and sinus bradycardia. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included acetylcysteine, amlodipine, buprenorphine, captopril, ceftazidime, chlorzoxazone, codeine, diphenhydramine, etoricoxib, fenoterol, gentamicin, ipratropium, meclozine, methylprednisolone, metoclopramide, morphine, pantoprazole, perindopril, prednisolone, prochlorperazine, serrapeptase, silybum marianum, terbutaline, theophylline, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right, left lobes of liver, tumor thrombus at left portal vein, and lymphadenopathy at the trifurcation of celiac trunk. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 08 Nov 2013 (Day 1), treatment with study drug was initiated.

On 26 Dec 2013 (Day 49), the subject was hospitalized for ruptured liver carcinoma (Grade 4) and also experienced musculoskeletal chest pain (Grade 2). On the same day (Day 49), CT of the abdomen showed tumor rupture at left lobe of liver causing hemoperitoneum and small amount of contrast extravasation. Laboratory tests showed ALT 75 U/L (NR: 10 – 50) and Hgb 12.1 g/dL (NR: 13.5 – 17). The subject underwent transcatheter arterial chemoembolization and was treated with ceftazidime, morphine, and tramadol. On 26 Dec 2013 (Day 49), the subject was withdrawn from study due to ruptured liver carcinoma secondary to clinical disease progression and received the last dose of the study drug on the same day. On 01 Jan 2014 (Day 55), the subject recovered from ruptured liver carcinoma. The subject did not recover from musculoskeletal chest pain. The Investigator considered ruptured liver carcinoma serious and not related to the study drug; musculoskeletal chest pain nonserious and not related to the study drug.

On 15 Jan 2014 (Day 69), the subject was hospitalized for metastases to spine (Grade 3). On 21 Jan 2014 (Day 75), nuclear magnetic resonance imaging of spine showed focal bony metastasis of S1 vertebral body. On 22 Jan 2014 (Day 76), the subject recovered from metastases to spine with sequelae. The Investigator considered metastases to spine serious and not related to the study drug.

On 13 Mar 2014 (Day 126, 77 days after the last dose), the subject died due to disease progression.

Subject Number	45021002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01448-CLI-TW
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Oesophageal varices haemorrhage

A 70-year-old Chinese female was diagnosed with hepatocellular carcinoma on 15 Oct 2013. Significant medical history included hepatic steatosis, gastric ulcer, hepatitis C, osteoarthritis (left shoulder), and spinal osteoarthritis (lumbar spondylosis). The subject did not receive any previous anticancer therapies. Prior and concomitant medications included atropine, bifidobacterium bifidum, bismuth, cefazolin, ciprofloxacin, colestyramine, dicycloverine, dimeticone, felodipine, furosemide, hyoscine, lansoprazole, lidocaine, loperamide, megestrol, pantoprazole, phytomenadione, pipoxolan, propranolol, silybum marianum, spironolactone, terlipressin, tranexamic acid, and vitamin B complex. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, mass at right 10th rib, and aortocaval and para-aortic lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 22 Nov 2013 (Day 1), treatment with study drug was initiated.

On 08 May 2014 (Day 168), tumor response assessment showed disease progression and the subject was withdrawn from the study due to disease progression. The subject received the last dose of study drug on the same day (Day 168).

On 20 May 2014 (Day 180), the subject was hospitalized for esophageal varices hemorrhage (Grade 3). Laboratory tests showed Hgb 10.1 g/dL (NR: 11.6 – 14), Hct 29.7% (NR: 34 – 44), platelet count 100 x10^9/L (NR: 150 – 400), and stool occult blood was positive 3+. Upper gastrointestinal tract endoscopy and paravariceal endoscopic sclerotherapy showed four esophageal varices over distal esophagus with signs of recent hemorrhage, esophago-cardiac junction variceal bleeding, and severe hypertensive gastropathy over gastric body and antrum with healing ulcer over antrum. The subject underwent esophageal variceal ligation and was also treated with packed red blood cell transfusion, terlipressin, tranexamic acid, pantoprazole, propranolol, and phytomenadione. On 30 May 2014 (Day 190), the subject recovered from esophageal varices hemorrhage. The Investigator considered esophageal varices hemorrhage serious and not related to the study drug.

On 08 Oct 2016 (Day 1052, 884 days after the last dose), the subject died due to disease progression.

Subject Number	45031009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-007909
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Pathological fracture

A 79-year-old Chinese male was diagnosed with hepatocellular carcinoma on 20 Dec 2012. Significant medical history included benign prostate hyperplasia, cataract, neurodermatitis, productive cough, dry eyes, blepharitis, hepatitis B, insomnia, maculopathy, pterygium, and gastroesophageal reflux disease. Previous anticancer therapies included epirubicin and transcatheter arterial chemoembolization. Prior and concomitant medications included amenol d, aminosteril hepa, amoxicillin, artificial tears, betamethasone, bromhexine, calcium, cefadroxil, cefazolin, cetirizine, chlorphenamine, clobetasol, clotrimazole, dialicon, dimeticone, entecavir, esomeprazole, etoricoxib, famotidine, fluclorolone acetonide, fluorometholone, fusidic acid, griseofulvin, hypromellose, lorazepam, magnesium oxide, megestrol, methylprednisolone, mitomycin, mosapride, mycomb, neomycin, pantoprazole, paracetamol, pethidine, sertaconazole, silvazine, silybum marianum, spironolactone, sulfadiazine, sulfamethoxazole, tamsulosin, tetanus vaccine, tramadol, ultracet, unacid, urea, valaciclovir, and zinc. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

On 09 Oct 2014 (Day 1), treatment with study drug was initiated.

On 08 Feb 2015 (Day 123), the subject experienced cutaneous vasculitis (Grade 3). Treatment included clotrimazole, mycomb, tramadol, unacid, amoxicillin, betamethasone, methylprednisolone, sulfadiazine, valaciclovir, zinc, cetirizine, fluclorolone acetonide, and neomycin. On 10 Feb 2015 (Day 125), the study drug was interrupted due to cutaneous vasculitis. On 16 Feb 2015 (Day 131), cutaneous vasculitis improved to Grade 2. On 24 Feb 2015 (Day 139), cutaneous vasculitis improved to Grade 1 and the study drug was resumed at reduced dose of 4 mg/day due to cutaneous vasculitis. On 12 Mar 2015 (Day 155), the subject recovered from the event. The Investigator considered cutaneous vasculitis nonserious and possibly related to study drug.

On 04 Apr 2015 (Day 178), the subject experienced pathological fracture (pathological T12 compression fracture; Grade 3) with symptom of back pain. On 04 May 2015 (Day 208), thoracic spine and lumbar spine x-rays showed pathological T12 compression fracture, anterior wedge deformity at L1, degenerative spondylolisthesis, and generalized osteoporosis. The subject was diagnosed with generalized osteoporosis (Grade 1) and spondylolisthesis (Grade 3). Treatment included etoricoxib, ultracet, and calcium. On 07 May 2015 (Day 211), the subject had bone mineral density test (results not provided). On 28 May 2015 (Day 232), the subject had MRI of lumbar spine (results not provided). On 08 Jun 2015 (Day 243), the subject was hospitalized for vertebroplasty. On 09 Jun 2015 (Day 244), the surgery was uneventful and the pathological fracture improved to Grade 1, and the subject was discharged from the hospital. The study drug dose was not changed. The

subject did not recover from spondylolisthesis, pathological fracture, and osteoporosis. The Investigator considered pathological fracture serious and not related to study drug; osteoporosis and spondylolisthesis nonserious and not related to study drug.

On 13 Jul 2015 (Day 278), tumor response assessment showed disease progression. On 16 Jul 2015 (Day 281), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 15 Jul 2015 (Day 280).

On 22 Nov 2015 (Day 410, 130 days after the last dose), the subject died due to disease progression.

Subject Number	45061006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003377
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Osteoarthritis, Jaundice cholestatic, Biliary tract infection

A 74-year-old Chinese male was diagnosed with hepatocellular carcinoma on 06 Nov 2013. Significant medical history included anemia, hepatitis B, hypertension, arthralgia (left knee pain), and chronic gastritis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included aciclovir, aldioxa, allopurinol, aminofluid, amlodipine, benzylpenicillin, bisacodyl, captopril, cefazolin, cefmetazole, celecoxib, chlorzoxazone, diclofenac, dimeticone, diphenhydramine, domperidone, dopamine, electrolytes w/glucose, estazolam, famotidine, fentanyl, fexofenadine, furosemide, human albumin, hydralazine, indometacin, iotalamate sodium w/ioxitalamate meglumine, ipratropium, lactulose, lipofundin, lorazepam, losartan, magnesium oxide, magnesium sulfate, manfugen, methylprednisolone, metoclopramide, morphine, mylanta, norepinephrine, paracetamol, piperacillin/tazobactam, piroxicam, senna alexandrina, sennoside a+b, sodium bicarbonate, sodium chloride, solutions for parenteral nutrition, sulperazon, tamsulosin, tolvaptan, ultracet, and urea. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of the liver. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 29 Nov 2013 (Day 1), treatment with study drug was initiated.

On 21 Nov 2014 (Day 358), the subject experienced osteoarthritis (Grade 2) and knee arthralgia (Grade 2). The subject was treated with ultracet, celecoxib, chlorzoxazone, and indometacin. On 01 Jan 2015 (Day 399), the study drug was interrupted due to osteoarthritis. On 07 Jan 2015 (Day 405), the subject was hospitalized due to worsening of osteoarthritis (Grade 3) and x-ray of knee showed obliteration of the left medial compartment and subchondral sclerosis compatible with end stage osteoarthritis. On 08 Jan 2015 (Day 406), the subject underwent total left knee arthroplasty and was treated with paracetamol. On 13 Jan 2015 (Day 411), the subject recovered from osteoarthritis. On 23 Jan 2015 (Day 421), the study drug was resumed at same dose of 12 mg/day. On 04 Mar 2015 (Day 461), the subject recovered from knee arthralgia. The Investigator considered osteoarthritis serious and not related to the study drug; knee arthralgia nonserious and not related to the study drug.

On 29 Sep 2015 (Day 670), the subject experienced increased gamma-glutamyltransferase (Grade 4). Laboratory tests showed ALP 490 U/L (NR: 43 – 115), ALT 284 U/L (NR: 10 – 40), AST 386 U/L (NR: 10 – 43), GGT 1728 U/L (NR: 10 – 49), and total bilirubin 36.3 umol/L (NR: 0 – 18.8). On 01 Oct 2015 (Day 672), the study drug was interrupted due to increased gamma-glutamyltransferase. On 06 Oct 2015 (Day 677), the subject experienced cholestatic jaundice (Grade 3) with total bilirubin 166.7 umol/L. On 07 Oct 2015 (Day 678), CT of abdomen confirmed obstructive jaundice. The subject was hospitalized and underwent bilateral percutaneous transhepatic cholangiodrainage with insertion of stents; and therapeutic

embolization with iotalamate sodium w/ioxitalamate meglumine, cefmetazole, fentanyl, electrolytes w/glucose, and sodium chloride. On 13 Oct 2015 (Day 684), the subject recovered from increased gamma-glutamyltransferase with GGT 626 U/L. On 16 Oct 2015 (Day 687), the subject experienced anemia (Grade 2) with Hgb 95 g/L (NR: 132 – 172) and was treated with packed red blood cell transfusion. On 18 Oct 2015 (Day 689), the subject experienced dyspnea (Grade 3), hypotension (Grade 1), and biliary tract infection (Grade 4) with fever that prolonged the hospitalization. On 19 Oct 2015 (Day 690), laboratory tests showed WBC 17.84 x10^9/L (NR: 3.54 – 9.06), neutrophil differential 94.3% (NR: 41.2 – 74.7). Blood culture showed bacteremia. The subject underwent central venous catheterization and was also treated with oxygen, paracetamol, piperacillin/tazobactam, solutions for parenteral nutrition, sodium chloride, dopamine, ipratropium, and norepinephrine. On 20 Oct 2015 (Day 691), the subject recovered from cholestatic jaundice with total bilirubin 32.1 umol/L. On 22 Oct 2015 (Day 693), the subject recovered from hypotension and on 25 Oct 2015 (Day 696), the subject recovered from dyspnea. On 26 Oct 2015 (Day 697), the study drug was resumed at a reduced dose of 8 mg/day due to increased gamma-glutamyltransferase. The subject was recovering from anemia. On 04 Nov 2015 (Day 706), the subject recovered from biliary tract infection and was discharged from the hospital. The Investigator considered cholestatic jaundice, biliary tract infection serious and not related to the study drug; increased gamma-glutamyltransferase nonserious and probably related to the study drug; anemia, dyspnea and hypotension nonserious and not related to the study drug.

On 24 Nov 2015 (Day 726), tumor response assessment showed disease progression. On 27 Nov 2015 (Day 729), the subject was withdrawn from study due to disease progression and received the last dose of study drug on the same day.

On 12 Feb 2016 (Day 806, 77 days after the last dose), the subject died due to disease progression.

Subject Number	45061015
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-007744
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Diarrhoea, Acute kidney injury, Bacteraemia, Salmonellosis

A 65-year-old Chinese male was diagnosed with hepatocellular carcinoma on 04 Mar 2013. Significant medical history included choledochotomy, constipation, hepatitis C, hypertension, and insomnia. Previous anticancer therapies included doxorubicin, hepatectomy, and transcatheter arterial chemoembolization. Prior and concomitant medications included aminofluid, amlodipine, bisacodyl, calcium chloride, cefotaxime, diosmectite, doxazosin, enalapril, flomoxef, furosemide, hydrotalcite, hyoscine, labetalol, lidocaine, losartan, magnesium oxide, megestrol, metoclopramide, mosapride, simeticone, sodium chloride, urea, and zolpidem. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe lung mass, multiple nodules in both lungs, and mediastinal lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 20 Jun 2014 (Day 1), treatment with study drug was initiated.

On 01 Jun 2015 (Day 347), the subject experienced diarrhea (Grade 2) and received unspecified supportive care. On 15 Jun 2015 (Day 361), the subject was hospitalized for persistent diarrhea, acute kidney injury (Grade 3), bacteremia (Grade 3), and salmonellosis (Grade 3). Laboratory tests were done and showed BUN 31.5231 mmol/L (NR: 1.6065 – 8.568), creatinine 406.64 umol/L (NR: 53.04 – 114.92), potassium 3.4 mmol/L (NR: 3.5 – 5.3), sodium 123 mmol/L (NR: 135 – 148), and fecal occult blood 1+; blood culture showed gram-negative bacillus and Salmonella; stool culture showed Salmonella and was negative for Clostridium difficile toxin. Blood pressure was 96/50 mmHg. The subject was treated with diosmectite, hyoscine, aminofluid, sodium chloride, flomoxef, and cefotaxime. On 16 Jun 2015 (Day 362), the study drug was interrupted due to these events. On 17 Jun 2015 (Day 363), the subject experienced hypocalcemia (Grade 2) with total calcium 1.99 mmol/L (NR: 2.02 – 2.6) and was treated with calcium chloride. The subject recovered from diarrhea on the same day (Day 363). On 22 Jun 2015 (Day 368), repeat laboratory tests showed BUN 4.6053 mmol/L, creatinine 79.56 umol/L, potassium 3.7 mmol/L, and sodium 140 mmol/L. On the same day (Day 368), the subject recovered from acute kidney injury. On 23 Jun 2015 (Day 369), the study drug was resumed at same dose of 12 mg/day. On 01 Jul 2015 (Day 377), the subject recovered from bacteremia and salmonellosis. The event of hypocalcemia was ongoing. The Investigator considered diarrhea, acute kidney injury, bacteremia, and salmonellosis serious and not related to the study drug; hypocalcemia nonserious and not related to the study drug.

On 29 Jun 2015 (Day 375), the subject experienced worsening of hypocalcemia (Grade 3) with total calcium 1.65 mmol/L. The subject was treated with calcium chloride and on 10 Jul 2015 (Day 386), the study drug was interrupted due to this event. On 14 Jul 2015 (Day 390), the subject recovered from hypocalcemia with total calcium 2.19 mmol/L. The Investigator considered hypocalcemia nonserious and not related to the study drug.

On 14 Jul 2015 (Day 390), tumor response assessment showed disease progression. On 17 Jul 2015 (Day 393), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 09 Jul 2015 (Day 385).

Subject Number	45071009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-011976
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Dengue fever

A 42-year-old Chinese male was diagnosed with hepatocellular carcinoma on 29 May 2014. Significant medical history included ascites, hepatitis B, and hepatic cirrhosis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included cefuroxime, dimeticone, diphenhydramine, hyoscine, ketorolac, lidocaine, loratadine w/pseudoephedrine, other emollients and protectives (actimed cream), paracetamol, ultracet, and uremol hc. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right and left lobes of the liver, and right lower lung nodules. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 24 Jul 2014 (Day 1), treatment with study drug was initiated.

On 06 Nov 2015 (Day 471), the subject experienced dengue fever (Grade 3). On 09 Nov 2015 (Day 474), the subject experienced decreased platelet count (Grade 3), decreased white blood cell count (Grade 2), and increased C-reactive protein (Grade 1). Laboratory tests showed platelets 27 x10^9/L (NR: 125 – 375), WBC 2 x10^9/L (NR: 3.7 – 11), and CRP 14.9 mg/L (NR: 0 – 5). On 11 Nov 2015 (Day 476), subject was hospitalized for dengue fever. Laboratory tests showed platelet count 9 x10^9/L (NR: 150 – 400) and WBC 3 x10^9/L (NR: 3.9 – 10.6). The subject was treated with paracetamol and platelet transfusion. On the same day (Day 476), the study drug was interrupted due to dengue fever and decreased platelet count. On 13 Nov 2015 (Day 478), the subject recovered from dengue fever and was discharged from the hospital. On 16 Nov 2015 (Day 481), the subject recovered from increased C-reactive protein, decreased platelet count, and decreased white blood cell count. Repeat blood test showed CRP 1.3 mg/L, platelet count 73 x10^9/L (NR: 125 – 375), and WBC 3.2 x10^9/L. On 18 Nov 2015 (Day 483), the study drug was resumed at same dose of 12 mg/day. The Investigator considered dengue fever serious and not related the study drug; increased C-reactive protein, decreased platelet count, and decreased white blood cell count nonserious and not related to the study drug.

On 12 Sep 2016 (Day 782), tumor response assessment showed disease progression. On 13 Oct 2016 (Day 813), the subject withdrew from the study due to disease progression and received the last dose on 12 Oct 2016 (Day 812).

Subject Number	45101002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01560-CLI-TW
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Fatigue, Decreased appetite (2x), Abdominal distension, Vomiting

A 63-year-old Chinese male was diagnosed with hepatocellular carcinoma on 10 Sep 2012. Significant medical history included diabetes mellitus, hepatitis B, hypertension, nephrolithiasis, and hepatic cirrhosis. Previous anticancer therapies included cisplatin, percutaneous ethanol injection, and transcatheter arterial chemoembolization. Prior and concomitant medications included acarbose, alprazolam, amlodipine, bisacodyl, ceftriaxone, celecoxib, dimeticone, diphenhydramine, esomeprazole, estazolam, flunitrazepam, furosemide, glimepiride, hyoscine, lactulose, levocetirizine, medroxyprogesterone, metformin, paracetamol, pioglitazone, potassium, ranitidine, sennoside a+b, simeticone, spironolactone, tamsulosin, terlipressin, ultracet, ursodeoxycholic acid, and zolpidem. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at quadrate, left, and right liver lobes; masses at right adrenal, right middle, and left lower lobes of lung. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 09 Jul 2014 (Day 1), treatment with study drug was initiated.

On 12 Jul 2014 (Day 4), the subject experienced decreased appetite (Grade 1). On 16 Jul 2014 (Day 8), the subject experienced fatigue (Grade 1). On 07 Aug 2014 (Day 30), the subject's decreased appetite and fatigue worsened to Grade 3. On 14 Aug 2014 (Day 37), the subject was hospitalized for decreased appetite and fatigue and the study drug was interrupted due to these events. On the same day (Day 37), the subject experienced abdominal distension (Grade 1). Treatment included furosemide. Laboratory tests showed AST 41 U/L (NR: 10 – 42), ALT 29 U/L (NR: 10 – 40), total bilirubin 31.464 umol/L (NR: 3.42 – 17.1), and albumin 30.9 g/L (NR: 35 – 50). On 15 Aug 2014 (Day 38), the subject was transfused with frozen plasma for nutritional support. On 18 Aug 2014 (Day 41), fatigue improved to Grade 2. On 19 Aug 2014 (Day 42), decreased appetite improved to Grade 2. On 21 Aug 2014 (Day 44), the subject experienced ascites (Grade 2). On 22 Aug 2014 (Day 45), fatigue improved to Grade 1. On 25 Aug 2014 (Day 48), laboratory tests showed albumin 36.5 g/L. On 25 Aug 2014 (Day 48), decreased appetite improved to Grade 1 and the subject experienced hypokalemia (Grade 3) with potassium 2.6 mmol/L (NR: not provided) and was treated with potassium. On 27 Aug 2014 (Day 50), the subject was discharged from the hospital and the study drug was resumed at reduced dose of 8 mg/day due to decreased appetite and fatigue. On the same day (Day 50), hypokalemia improved to Grade 1. On 29 Aug 2014 (Day 52), the subject recovered from hypokalemia with potassium 3.8 mmol/L (NR: 3.5 – 5). The subject did not recover from ascites. The Investigator considered decreased appetite, fatigue serious and probably related to study drug; ascites nonserious and possibly related to study drug; abdominal distension and hypokalemia nonserious and not related to study drug.

On 26 Sep 2014 (Day 80), the subject experienced hypoalbuminemia (Grade 1) and proteinuria (Grade 2). Laboratory tests showed albumin 31 g/L (NR: 35 – 55) and urine protein dipstick 2+. On 02 Oct 2014 (Day 86), the subject experienced abdominal distension (Grade 2). On 06 Oct 2014 (Day 90), decreased appetite worsened to Grade 2 and subject experienced vomiting (Grade 2). Treatment included medroxyprogesterone. On 08 Oct 2014 (Day 92), the subject recovered from vomiting. On 09 Oct 2014 (Day 93), the subject was hospitalized for vomiting and abdominal distension for further management and no vomiting was noted on that day. On the same day (Day 93), hypoalbuminemia worsened to Grade 2 with albumin 26.9 g/L (NR: 35 – 50). The subject was transfused with frozen plasma. On 09 Oct 2014 (Day 93), the subject withdrew from the study on subject's choice and received the last dose on 08 Oct 2014 (Day 92). On 13 Oct 2014 (Day 97), decreased appetite improved to Grade 1. On 15 Oct 2014 (Day 99), the subject recovered from proteinuria with 24h urine protein 0.868 g/24hr. On 20 Oct 2014 (Day 104), the subject recovered from hypoalbuminemia with albumin 34.7 g/L (NR: 35 – 50). On 21 Oct 2014 (Day 105), the subject recovered from fatigue and decreased appetite. On 22 Oct 2014 (Day 106), the subject experienced abdominal distension (Grade 1). Treatment included spironolactone and furosemide. On the same day (Day 106), the subject was discharged from the hospital with the outcome of abdominal distension recovering. On 23 Oct 2014 (Day 107), Child Pugh score was 8. The Investigator considered vomiting serious and probably related to study drug; abdominal distension serious and not related to study drug; decreased appetite nonserious and probably related to study drug; hypoalbuminemia and proteinuria nonserious and possibly related to study drug.

On 31 Oct 2014 (Day 115), the abdominal distension worsened to Grade 2. On 03 Nov 2014 (Day 118), the subject experienced decreased appetite (Grade 3). On 06 Nov 2014 (Day 121), the subject was re-hospitalized for decreased appetite and abdominal distension. On 06 Nov 2014 (Day 121), abdominal ultrasound showed mild ascites and ileus. On 11 Nov 2014 (Day 126), the subject had ultrasound guided paracentesis. On 12 Nov 2014 (Day 127), the subject had a black stool passage and coffee ground vomiting. The subject underwent gastric lavage and the subject was diagnosed with upper gastrointestinal hemorrhage (Grade 3). Treatment included esomeprazole, terlipressin, and packed RBC transfusion. The subject did not recover from abdominal distension, decreased appetite, and upper gastrointestinal hemorrhage. The Investigator considered decreased appetite and abdominal distension serious and not related to study drug; upper gastrointestinal hemorrhage nonserious and not related to study drug.

On 13 Nov 2014 (Day 128, 36 days after the last dose), the subject died due to disease progression. Autopsy was not performed.

Subject Number	46031005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01535-CLI-PH
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Pneumonia

A 59-year-old Asian male was diagnosed with hepatocellular carcinoma on 05 May 2014. Significant medical history included cancer pain and hepatitis B. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included augmentin, azithromycin, clevudine, hyoscine, mupirocin, norgesic, paracetamol, phospholipids, piperacillin/tazobactam, and ultracet. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe. The BCLC Stage was B, ECOG performance was 0, and Child Pugh score was 6.

On 31 May 2014 (Day 1), treatment with study drug was initiated.

On 31 May 2014 (Day 1), the subject experienced oropharyngeal pain (Grade 1). On 02 Jun 2014 (Day 3), the subject experienced pyrexia (Grade 1). On 02 Jun 2014 (Day 3), the study drug was interrupted due to pyrexia and oropharyngeal pain. On 02 Jun 2014 (Day 3), the subject recovered from pyrexia. On 03 Jun 2014 (Day 4), the subject recovered from oropharyngeal pain, and the study drug was resumed at a reduced dose of 8 mg/day due to these events. The Investigator considered pyrexia and oropharyngeal pain nonserious and possibly related to study drug.

On 28 Jun 2014 (Day 29), the subject experienced pneumonia (Grade 3), decreased appetite (Grade 1), malaise (Grade 1), and pyrexia (Grade 1) with body temperature of 37.1 ºC. Treatment included norgesic, hyoscine, augmentin, paracetamol, piperacillin/tazobactam, and azithromycin. On 03 Jul 2014 (Day 34), the subject was hospitalized due to pneumonia with body temperature of 39 ºC, and chest x-ray showed chronic inflammatory process in the left upper lobe compatible with pulmonary tuberculosis with fibrosis and volume loss. On 03 Jul 2014 (Day 34), the subject withdrew from the study by choice and received the last dose of the study drug on 28 Jun 2014 (Day 29). On 09 Jul 2014 (Day 40), the subject was discharged from the hospital. On 10 Jul 2014 (Day 41), the subject recovered from decreased appetite, pneumonia, and pyrexia. On 11 Jul 2014 (Day 42), the subject recovered from malaise. The Investigator considered pneumonia serious and probably related to study drug and disease progression; decreased appetite and pyrexia nonserious and possibly related to study drug and disease progression; malaise nonserious and possibly related to study drug.

On 17 Jul 2015 (Day 413, 384 days after the last dose), the subject died and it was unknown if death was due to disease progression.

Subject Number	46041004
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000464
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Oesophageal varices haemorrhage, Lung infection, Hepatic cirrhosis

A 59-year-old Asian male was diagnosed with hepatocellular carcinoma on 07 Aug 2014. Significant medical history included alcoholism, type 2 diabetes mellitus, hypertension, and hepatic cirrhosis. The subject did not receive any previous anti-cancer therapies. Prior and concomitant medications included acetylcysteine, amino acids w/carbohydrates, aminoleban, budesonide, ceftazidime, ciprofloxacin, clonidine, co-trimoxazole, diphenhydramine, enalapril, enoxaparin, furosemide, gliclazide, human albumin, hydrocortisone, insulin glargine, insulin glulisine, ipratropium, lactulose, lansoprazole, menadione, meropenem, metformin, metoclopramide, metronidazole, naproxen, nicardipine, nifedipine, octreotide, ornithine, pantoprazole, paracetamol, phytomenadione, piperacillin/tazobactam, propranolol, simeticone, sodium bicarbonate, spironolactone, sulfamethoxazole, terlipressin, and vasopressin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe and multiple bilateral lung nodules. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 06 Sep 2014 (Day 1), treatment with study drug was initiated.

On 26 Sep 2014 (Day 21), the subject experienced hematemesis (approximately 500 ml). The subject was brought to the emergency room and was found to be unresponsive with stable vital signs and later subject's blood pressure increased and oxygen saturation decreased to 70%. The subject was diagnosed with esophageal varices hemorrhage (Grade 4) and was hospitalized for lung infection (Grade 3). The subject was intubated and placed on ventilator support. Treatment included octreotide, terlipressin, vasopressin, amino acids w/carbohydrates, and pantoprazole, and the study drug was interrupted due to these events. On 27 Sep 2014 (Day 22), the subject woke up and was restless with spontaneous movements. The subject's BP was 159/91 mmHg. The subject was also diagnosed with hepatic cirrhosis (Grade 3) which prolonged hospitalization. Laboratory tests showed albumin 23 g/L (NR: 34 – 50), AST 69 U/L (NR: 15 – 37), ALT 46 U/L (NR: 12 – 78), ALP 155 U/L (NR: 50 – 136), RBC 4.62 x10^12/L (NR: 4.7 – 6.1), Hgb 145 g/L (NR: 130 – 170), and Hct 0.404 L/L (NR: 0.4 – 0.52). Additional treatment included total parenteral nutrition, metronidazole, lactulose, ornithine, and nicardipine. On 29 Sep 2014 (Day 24), the subject recovered from esophageal varices hemorrhage. On the same day (Day 24), the subject experienced sinus tachycardia (Grade 1) with HR of 136 bpm and ventricular extrasystoles (Grade 1) confirmed by electrocardiogram. Chest x-ray showed new infiltrates on left lower lung which was considered as ventilator associated pneumonia. On the same day (Day 24), the subject also developed bacterial gastroenteritis (Grade 2) with a positive C. difficile on stool examination and recovered from sinus tachycardia and ventricular extrasystoles. Additional treatments included piperacillin/tazobactam, ipratropium, and propranolol. On 30 Sep 2014 (Day 25), an endotracheal aspirate showed Staphylococcus species and repeat chest x-ray showed decreased infiltrates in the left lower lung. On the same day

(Day 25), the subject recovered from bacterial gastroenteritis. On 01 Oct 2014 (Day 26), the subject experienced hepatic encephalopathy (Grade 2) and was treated with aminoleban. On 02 Oct 2014 (Day 27), repeat chest x-ray showed regression of left lower lung opacities and the subject's ventilator was shifted to synchronized intermittent mandatory ventilation mode. The subject's lung infection was improving and the subject was eventually extubated and was placed on oxygen support. On 03 Oct 2014 (Day 28), the subject recovered from lung infection and hepatic encephalopathy. On 07 Oct 2014 (Day 32), the subject experienced increased shortness of breath, tachypnea, spoke in short phrases, and complained of feeling bloated with minimal relief after simeticone. Abdominal girth was measured at 109 cm and intravenous fluids were discontinued. The subject underwent scout film of abdomen and chest x-ray. An abdominal ultrasound showed 783 cc of ascitic fluid. On the same day (Day 32), the subject experienced peripheral edema (bipedal edema; Grade 2) and hypoalbuminemia (Grade 3) with albumin 17 g/L. The subject was treated with spironolactone, human albumin, and furosemide. Complete blood count revealed WBC 14.7 x10^9/L (NR: 4.8 – 10.8) and differential neutrophil count 89% (NR: 40 – 74). On 09 Oct 2014 (Day 34), arterial blood gas showed metabolic acidosis and repeat chest x-ray showed slight regression of bilateral pulmonary congestive changes on upper lung fields. The subject was treated with sodium bicarbonate drip and a repeat arterial blood gas showed respiratory alkalosis. On same day (Day 34), the subject recovered from peripheral edema and hypoalbuminemia. On 14 Oct 2014 (Day 39), repeat abdominal ultrasound showed 1385.4 cc of ascitic fluid and minimal pleural effusion on the left lung. On 16 Oct 2014 (Day 41), the subject underwent paracentesis and 2.5 L of yellowish fluid was drained. The subject tolerated the procedure well with no postoperative complications and the ascitic fluid indicated portal hypertension as the etiology. On 20 Oct 2014 (Day 45), a repeat abdominal ultrasound showed 1 L of ascitic fluid. On 21 Oct 2014 (Day 46), the subject was started to be weaned off the oxygen. On 23 Oct 2014 (Day 48), the subject was discharged from the hospital. The subject did not recover from hepatic cirrhosis. The Investigator considered esophageal varices hemorrhage, hepatic cirrhosis, and lung infection serious and probably related to study drug; ventricular extrasystoles nonserious and possibly related to study drug; hepatic encephalopathy, peripheral edema, hypoalbuminemia, bacterial gastroenteritis, and sinus tachycardia nonserious and not related to study drug.

On 06 Nov 2014 (Day 62), the subject withdrew from the study by choice and received the last dose of the study drug on 26 Sep 2014 (Day 21).

On 28 Dec 2014 (Day 114, 93 days after the last dose), the subject died and the cause of death was unknown. Autopsy was not performed.

Subject Number	47021009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-013056
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Gastric ulcer, Tumour haemorrhage

A 51-year-old Chinese male was diagnosed with hepatocellular carcinoma on 27 Jun 2013. Significant medical history included chronic duodenal ulcer, chronic hepatitis B, and hepatic cirrhosis. Previous anticancer therapies included radiotherapy to segment V and VIII of liver, ethanol ablation segment IV of liver, and hepatectomy (left lateral sectionectomy). Prior and concomitant medications included chlorphenamine, domperidone, entecavir, famotidine, furosemide, hypromellose, ketorolac, lactulose, pantoprazole, paracetamol, salicylic acid, senna alexandrina, tramadol, tranexamic acid, and urea. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at segments I and V of liver, para-caval lymphadenopathy, and omental mass. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 31 Dec 2014 (Day 1), treatment with study drug was initiated.

On 27 Nov 2015 (Day 332), tumor response assessment showed disease progression. On 03 Dec 2015 (Day 338), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on the same day.

On 17 Dec 2015 (Day 352), the subject was hospitalized for acute gastric ulcer (Grade 3) and stomach tumor hemorrhage (Grade 3) which was confirmed on esophagogastroduodenoscopy. On the same day (Day 352), the subject also experienced anemia (Grade 3), shortened activated partial thromboplastin time (Grade 1), and prolonged prothrombin time (Grade 1). Laboratory tests showed PT 13.7 sec (NR: 10.4 – 12.6), RBC 1.12 x10^12/L (NR: 4.3 – 5.7), and Hgb 39 g/L (NR: 134 – 172). The subject was treated with furosemide, chlorphenamine, pantoprazole, tranexamic acid, tramadol, and multiple blood transfusions. On 19 Dec 2015 (Day 354), the subject recovered from shortened activated partial thromboplastin time and anemia improved to Grade 2 with Hgb 96 g/L. On 23 Dec 2015 (Day 358), the subject's general condition was stable and the subject was discharged from hospital. On 24 Dec 2015 (Day 359), the subject underwent palliative hemostatic radiotherapy to the stomach tumor and after the procedure the subject was re-admitted for coffee colored vomiting. On 26 Dec 2015 (Day 361), severity of anemia worsened to Grade 3 with Hgb 75 g/L. On 28 Dec 2015 (Day 363), the subject recovered from prolonged prothrombin time with PT 12.7 sec. On the same day (Day 363), repeat esophagogastroduodenoscopy showed necrotic tumor at fundus without bleeding, minimal contact bleeding after normal saline flushing and failed duodenal intubation due to tumor obstruction. On the same day (Day 363), anemia improved to Grade 2 with Hgb 96 g/L. On 31 Dec 2015 (Day 366), the severity of acute gastric ulcer improved to Grade 1. On the same day (Day 366), the subject recovered from stomach tumor hemorrhage and was discharged from the hospital. The subject did not recover from acute gastric ulcer. The Investigator considered acute gastric ulcer serious and not related to the study drug but related to

disease progression; tumor hemorrhage serious and not related to the study drug; anemia, prolonged prothrombin time, and shortened activated partial thromboplastin time nonserious and not related to the study drug.

On 13 May 2016 (Day 500, 162 days after the last dose), the subject died due to disease progression.

Subject Number	47031003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-020676
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Dizziness

A 78-year-old Chinese male was diagnosed with hepatocellular carcinoma on 08 Sep 2003. Significant medical history included constipation, gastroesophageal reflux disease, hepatitis B, and bladder obstruction. Previous anticancer therapies included hepatectomy (3x) and transcatheter arterial chemoembolization. Prior and concomitant medications included amlodipine, betadermic, calcium d3, chlorphenamine, entecavir, fluocinolone acetonide, hydroxyzine, loperamide, marsedyl, maxitrol, megestrol, mometasone, other emollients and protectives (aqueous cream, emulsifying ointment), oxybutynin, pantoprazole, paracetamol, prochlorperazine, pyridoxine, senna alexandrina, tamsulosin, timolol, and valsartan. At Screening, tumor assessments of target/non-target lesions via CT scan showed left adrenal, omentum, between the left renal vein & pancreatic tail, and left adrenal bed lateral masses. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 23 Jan 2014 (Day 1), treatment with study drug was initiated.

On 18 Sep 2016 (Day 970), the subject was hospitalized for dizziness (Grade 3). Diagnostic tests were performed and electrocardiogram, chest x-ray, and brain CT scan were normal. The subject was treated with prochlorperazine. On 19 Sep 2016 (Day 971), the subject recovered from dizziness. The Investigator considered dizziness serious and not related to the study drug.

The subject remained in the study at the time of data cut-off.