Subject Number	21021001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01451-CLI-ES
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Gastrointestinal haemorrhage
AE(s) Leading to Discontinuation	Gastrointestinal haemorrhage

A 78-year-old white male was diagnosed with hepatocellular carcinoma in Dec 2011. Significant medical history included actinic keratosis, anemia, atrial fibrillation, chronic obstructive pulmonary disease, mitral valve incompetence, emphysema, esophageal varices, gastrointestinal hemorrhage, hepatitis C, nephrolithiasis, and portal hypertension. Previous anticancer therapies included hepatic regional chemotherapy, high frequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included ceftriaxone, deflazacort, enoxaparin, fluticasone, furosemide, haloperidol, iron, lactulose, metoclopramide, omeprazole, pantoprazole, paracetamol, phytomenadione, proctosol, propranolol, salmeterol, and somatostatin. At Screening, tumor assessments of target/non-target lesions via CT scan showed a lesion at left liver lobe and mediastinal lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 7.

On 12 Feb 2014 (Day 1), treatment with study drug was initiated.

On 13 Feb 2014 (Day 2), the subject was hospitalized for gastrointestinal hemorrhage (Grade 4). On 14 Feb 2014 (Day 3), the study drug was interrupted due to this event. Laboratory test showed Hgb 63 g/L (NR: 120 – 160) and PT 14 sec (NR: 10 – 14). The subject was treated with gastric banding via endoscopy, red blood cell transfusion, iron, phytomenadione, and pantoprazole. On 25 Feb 2014 (Day 14), the subject recovered from gastrointestinal hemorrhage with Hgb 118 g/L, Hct 0.36 L/L (NR: 0.36 – 0.46), and RBC 4.4 x10^12/L (NR: 4 – 5.5). On 07 Mar 2014 (Day 24), the subject was withdrawn from the study due to this event and received the last dose of study drug on 13 Feb 2014 (Day 2). The Investigator considered gastrointestinal hemorrhage serious and not related to study drug.

On 31 Mar 2014 (Day 48), the tumor response assessment showed disease progression.

On 03 May 2014 (Day 81), the subject experienced multiple organ dysfunction syndrome (Grade 4). On 10 May 2014 (Day 88, 86 days after the last dose), the subject died due to multiple organ dysfunction syndrome. The Investigator considered multiple organ dysfunction syndrome serious and not related to the study drug but related to disease progression.

Subject Number	24021003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01553-CLI-CN
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Encephalopathy
AE(s) Leading to Discontinuation	Encephalopathy

A 41-year-old Chinese female was diagnosed with hepatocellular carcinoma in Oct 2013. Significant medical history included chronic hepatitis B and liver biopsy. Previous anticancer therapies included radiotherapy to right liver lobe and bilateral lungs, palliative intervention therapy, and unspecified herbal and traditional medicine (cinobufagin). Prior and concomitant medications included human albumin, amino acids, amino acids with polypeptide, carthamus tinctorius, dexamethasone, diazepam, entecavir, furosemide, glutathione, lidocaine, mannitol, methylprednisolone, metoclopramide, morphine, omeprazole, ondansetron, pantoprazole, potassium, torasemide, unspecified herbal and traditional medicine (suxiao jiuxin), and vitamin B-complex with vitamin C. At Screening, tumor assessments of target/non-target lesions via CT scan showed masses at bilateral lungs and lesion at right liver lobe. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 11 Jun 2014 (Day 1), treatment with study drug was initiated.

On 02 Aug 2014 (Day 53), the subject was hospitalized for encephalopathy (Grade 4) and the study drug was interrupted due to this event. On 07 Aug 2014 (Day 58), the study drug was resumed at same dose. On 10 Aug 2014 (Day 61), the study drug was interrupted due to encephalopathy. On 13 Aug 2014 (Day 64), the subject experienced abdominal pain (Grade 1) and decreased weight (Grade 2). On 14 Aug 2014 (Day 65), the subject experienced increased aspartate aminotransferase (Grade 1), decreased blood albumin (Grade 2), and hyponatremia (Grade 3). Laboratory tests showed AST 100.6 U/L (NR: 13 – 35), ALP 253.9 U/L (NR: 50 – 135), total bilirubin 22.6 umol/L (NR: 5.7 – 27), albumin 23.7 g/L (NR: 40 – 55), sodium 129.3 mmol/L (NR: 137 – 147), and GGT 283.5 U/L (NR: 7 – 45). On 14 Aug 2014 (Day 65), head CT scan showed a new lesion on the brain and tumor response assessment showed disease progression. On 15 Aug 2014 (Day 66), the subject was withdrawn from the study due to disease progression. The subject received the last dose of the study drug on 10 Aug 2014 (Day 61). On 15 Aug 2014 (Day 66), the hyponatremia improved to Grade 1 with sodium 130 mmol/L (NR: 133 – 145). The subject was treated with mannitol, dexamethasone, morphine, furosemide, glutathione, torasemide, diazepam, and methylprednisolone. On 20 Aug 2014 (Day 71), the encephalopathy improved to Grade 2. On 22 Aug 2014 (Day 73), subject experienced abdominal distention (Grade 2). The subject did not recover from encephalopathy, abdominal pain, decreased weight, increased aspartate aminotransferase, decreased blood albumin, hyponatremia, and abdominal distention. The Investigator considered encephalopathy serious and not related to the study drug but related to disease progression; abdominal pain, decreased weight, increased aspartate aminotransferase, decreased blood albumin, hyponatremia and abdominal distention nonserious and not related to the study drug.

On 13 Sep 2014 (Day 95, 34 days after the last dose), the subject died due to disease progression.

Subject Number	24041009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-005522
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Vertigo

A 34-year-old Chinese male was diagnosed with hepatocellular carcinoma in Nov 2012. Significant medical history included cholecystectomy and hepatitis B. Previous anticancer therapies included hepatectomy and high frequency ablation. The subject did not receive any prior or concomitant medications. At Screening, tumor assessments of target/non-target lesions via CT scan showed masses at right upper and lower lung lobes. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 21 Aug 2014 (Day 1), treatment with study drug was initiated.

On 14 Mar 2015 (Day 206), the subject was hospitalized for vertigo (Grade 3) and also experienced nausea (Grade 3) and vomiting (Grade 3). On 15 Mar 2015 (Day 207), head CT scan showed no abnormalities. The subject was treated with unknown medications. On 01 Apr 2015 (Day 224), brain MRI showed dual lateral ventricle branch into centrum semiovale and updotted demyelination. On 03 Apr 2015 (Day 226), the severity of vertigo, nausea, and vomiting improved to Grade 1. On 14 May 2015 (Day 267), the subject recovered from vertigo, nausea, and vomiting. The study drug dose did not change. The Investigator considered vertigo serious and not related to the study drug; nausea and vomiting nonserious and possibly related to the study drug.

On 03 Mar 2016 (Day 561), tumor response assessment showed disease progression. On 05 Mar 2016 (Day 563), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on the same day (Day 563).

Subject Number	24041014
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003408
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Platelet count decreased

A 58-year-old Chinese female was diagnosed with hepatocellular carcinoma on 15 Sep 2014. Significant medical history included hepatic cirrhosis. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included amino acids w/polypeptide, menadione, and unspecified herbal and traditional medicine (compound zaofan). At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left liver lobe and other lesions in liver. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 04 Dec 2014 (Day 42), the subject experienced decreased platelet count (Grade 3). Laboratory tests showed platelet count 34 x10^9/L (NR: 125 – 375), RBC 4.15 x10^12/L (NR: 3.7 – 5.2), WBC 5.8 x10^9/L (NR: 3.7 – 11), Hgb 121 g/L (NR: 110 – 155), and absolute neutrophil count 3.6 x10^9/L (NR: 1.7 – 7.9). Treatment included amino acids w/polypeptide, menadione, and unspecified herbal and traditional medicine (compound zaofan). The subject did not recover from decreased platelet count and the study drug dose did not change. The Investigator considered decreased platelet count nonserious and possibly related to the study drug.

On 19 Jan 2015 (Day 88), decreased platelet count worsened to Grade 4 with platelet count 17 x10^9/L (NR: not provided). The subject was hospitalized and was transfused with platelets. On 25 Jan 2015 (Day 94), the severity of decreased platelet count improved to Grade 3 with platelet count 33 x10^9/L (NR: not provided). On 26 Jan 2015 (Day 95), the study drug was interrupted due to decreased platelet count. On 10 Feb 2015 (Day 110), the severity of decreased platelet count improved to Grade 2 with platelet count 58 x10^9/L (NR: not provided). The subject was recovering from the event. The Investigator considered decreased platelet count serious and possibly related to the study drug.

On 05 Mar 2015 (Day 133), the study drug was resumed at an unknown dose by the subject. On 30 Mar 2015 (Day 158), the subject was withdrawn from the study due to Investigator's decision and received the last unknown dose on the same day (Day 158). The subject received the last known dose of the study drug on 25 Jan 2015 (Day 94).

On 22 Oct 2015 (Day 364, 206 days after the last dose), the subject died due to disease progression.

Subject Number	24071003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000038
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Jaundice
AE(s) Leading to Discontinuation	Jaundice

A 39-year-old Chinese male was diagnosed with hepatocellular carcinoma on 10 Jun 2014. Significant medical history included hepatitis B and hepatic cirrhosis. Previous anticancer therapies included unspecified herbal and traditional medicine (jinke huaier granule) and hepatectomy. Prior and concomitant medications included ademetionine, biapenem, ceftizoxime, estazolam, glucose injection, glutathione, glycyrrhizic acid, human albumin, lamivudine, meglumine adenosine cyclophosphate, myrtol, ornithine, pantoprazole, polyene phosphatidylcholine, sodium chloride, spironolactone, thymalfasin, and vitamins. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes; bilateral lung masses; and left upper cervical lymphadenopathy. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 05 Sep 2014 (Day 1), treatment with study drug was initiated.

On 09 Sep 2014 (Day 5), the subject was hospitalized for jaundice (Grade 3). Laboratory tests showed total bilirubin 301 umol/L (NR: 5 – 22), ALT 136 U/L (NR: 9 – 50), and AST 123 U/L (NR: 15 – 40). Abdominal CT scan did not show any abnormalities. The subject was treated with ademetionine, glutathione, ornithine, polyene phosphatidylcholine, and glycyrrhizic acid. On 13 Sep 2014 (Day 9), repeat laboratory tests showed albumin 34.5 g/L (NR: 40 – 55), ALT 66 U/L, AST 83 U/L, ALP 346 U/L (NR: 45 – 125), and total bilirubin 715 umol/L. On 19 Sep 2014 (Day 15), the subject was withdrawn from the study due to jaundice. The subject received the last dose of the study drug on 10 Sep 2014 (Day 6). The subject did not recover from jaundice. The Investigator considered jaundice serious and possibly related to the study drug.

Subject Number	24101001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000969
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Ascites (2x)

An 81-year-old Chinese male was diagnosed with hepatocellular carcinoma on 12 Jul 2013. Significant medical history included hepatitis C, hypertension, hepatic cirrhosis, and supraventricular tachycardia. Previous anticancer therapies included transcatheter arterial chemoembolization (4x). Prior and concomitant medications included aldactazide a, glutathione, glycyrrhizic acid, human albumin, nifedipine, ornithine, and tiopronin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe and ascites. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 25 Jul 2014 (Day 1), treatment with study drug was initiated.

On 08 Oct 2014 (Day 76), the subject experienced ascites (Grade 3) and ultrasound of abdomen confirmed ascites. On 15 Oct 2014 (Day 83), the subject was hospitalized for ascites and was treated with tiopronin, glutathione, and aldactazide a. The study drug dose did not change. On 21 Oct 2014 (Day 89), the subject recovered from ascites and was discharged from the hospital. The Investigator considered ascites serious and possibly related to the study drug.

On 06 Jan 2015 (Day 166), the subject experienced another episode of ascites (Grade 3). On 08 Jan 2015 (Day 168), the subject was hospitalized for ascites. Laboratory results showed AST 117 U/L (NR: 0 – 50), ALP 113 U/L (NR: 30 – 120), albumin 32.7 g/L (NR: 35 – 52), and total bilirubin 32 umol/L (NR: 5 – 21). The subject was treated with tiopronin, glutathione, aldactazide a, ornithine, glycyrrhizic acid, and human albumin. The study drug dose did not change. On 17 Jan 2015 (Day 177), the subject recovered from ascites. The Investigator considered ascites serious and possibly related to the study drug.

On 09 Jan 2015 (Day 169), tumor response assessment showed disease progression. On 14 Jan 2015 (Day 174), the subject was withdrawn from the study due to disease progression and received last dose of study drug on the same day (Day 174).

Subject Number	24101003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-010270
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Hepatic function abnormal

A 42-year-old Chinese male was diagnosed with hepatocellular carcinoma on 20 Oct 2013. Significant medical history included hepatitis B. Previous anticancer therapies included transcatheter arterial chemoembolization (3x). Prior and concomitant medications included ademetionine, bicyclol, glutathione, glycyrrhizic acid, human albumin, hydrochloric acid, polyene phosphatidylcholine, spironolactone, and tiopronin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 25 Jul 2014 (Day 1), treatment with study drug was initiated.

On 24 Jun 2015 (Day 335), the subject experienced increased aspartate aminotransferase (Grade 3) with AST 268 U/L (NR: 10 – 43) and was treated with bicyclol and tiopronin. The study drug dose did not change and the subject did not recover from this event. The Investigator considered increased aspartate aminotransferase nonserious and probably related to the study drug.

On 21 Aug 2015 (Day 393), the subject was hospitalized for abnormal hepatic function (Grade 3). Laboratory results showed albumin 31 g/L (NR: 35 – 55), ALP 360 U/L (NR: 43 – 115), ALT 58 U/L (NR: 10 – 40), AST 577 U/L, total bilirubin 33.2 umol/L (NR: 0 – 18.8), and GGT 204 U/L (NR: 10 – 49). The subject was treated with glutathione, tiopronin, glycyrrhizic acid, polyene phosphatidylcholine, ademetionine, human albumin, hydrochloric acid, and spironolactone. The subject was recovering from this event. The Investigator considered abnormal hepatic function serious and possibly related to the study drug and related to disease progression.

On 21 Aug 2015 (Day 393), tumor response assessment showed disease progression. On 31 Aug 2015 (Day 403), the subject was withdrawn from study due to disease progression and received the last dose of study drug on the same day.

Subject Number	24101010
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-002027
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Cholecystitis acute, Cardiac failure
AE(s) Leading to Discontinuation	Cardiac failure

A 66-year-old Chinese female was diagnosed with hepatocellular carcinoma on 13 Dec 2013. Significant medical history included hepatitis C and hepatic cirrhosis. Previous anticancer therapies included radiotherapy to left rib lesion and transcatheter arterial chemoembolization (3x). Prior and concomitant medications included adenosine-5'-triphosphategluconate-magnesium, alanyl glutamine, ambroxol, amino acids, amiodarone, cefodizime, dexamethasone, diphenhydramine, escin, estazolam, felodipine, filgrastim, general nutrients, glutathione, glycerol, glyceryl trinitrate, granulocyte colony stimulating factor, human albumin, ipratropium, iron, isosorbide mononitrate, lactulose, levocarnitine, ligustrum lucidum, metoprolol, omeprazole, ornithine, potassium, unspecified herbal and traditional medicine (dan shen shuan xiong qin, kang ai, li dan pian, bozhi glycopeptide), vitamins, other combinations (lipid-soluble vitamin II). At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe; left upper lobe lung mass. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 03 Sep 2014 (Day 1), treatment with study drug was initiated.

On 25 Nov 2014 (Day 84), the subject was hospitalized for acute cholecystitis (Grade 3) and the study drug was interrupted due to this event. The subject underwent cholangistomy and was treated with cefodizime, glutathione, omeprazole, unspecified herbal and traditional medicine (kang ai, dan shen shuan xiong qin, li dan pian, bozhi glycopeptide), ambroxol, ipratropium, levocarnitine, and escin. On 28 Nov 2014 (Day 87), the study drug was resumed at same dose. On 04 Dec 2014 (Day 93), the subject recovered from acute cholecystitis. The Investigator considered acute cholecystitis serious and not related to the study drug.

On 08 Mar 2015 (Day 187), the subject was hospitalized for cardiac failure (Grade 1). Electrocardiogram showed anterior wall myocardial infarction, prolonged QT interval, and T wave inversion of I/II/aVL/v1–v6. Laboratory tests showed creatinine kinase 5.28 ng/mL (NR: not provided), myoglobin 286.23 ng/mL (NR: not provided), and high sensitivity troponin 5.374 ng/mL (NR: not provided). The subject was treated with adenosine-5'-triphosphategluconate-magnesium, cefodizime, dexamethasone, isosorbide mononitrate, ligustrum lucidum, levocarnitine, ornithine, potassium, amiodarone, glutathione, and metoprolol. On 10 Mar 2015 (Day 189), the study drug was interrupted due to this event. On 17 Mar 2015 (Day 196), the subject was withdrawn from the study due to cardiac failure and received the last dose of the study drug on 09 Mar 2015 (Day 188). On 09 May 2015 (Day 249), the subject recovered from this event. The Investigator considered cardiac failure serious and possibly related to the study drug. The Investigator stated that the ECG findings may not be accurate and myocardial infarction was not an adverse event.

Subject Number	24131003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01517-CLI-CN
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Pathological fracture

A 64-year-old Chinese female was diagnosed with hepatocellular carcinoma on 24 Jan 2014. Significant medical history included abdominal pain, arrhythmia, gastritis, hepatic steatosis, hepatitis B, and renal cyst. Previous anticancer therapies included epirubicin, mitomycin, oxaliplatin, and transcatheter arterial chemoembolization. Prior and concomitant medications included ademetionine, bacillus lichenformis, berberine, bifidobacterium animalis w/lactobac, dexamethasone, diclofenac, general nutrients, glycerol, glycyrrhizic acid, ligustrazine, loperamide, montmorillonite, nitrendipine, omeprazole, oxycodone, pantoprazole, phenolphthalein, sulperazon, thymopentin, and unspecified herbal and traditional medicine (hongjingtian, qizhen, bianmishu, and guhong). At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe and para-aortic lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 21 Apr 2014 (Day 1), treatment with study drug was initiated.

On 03 Jun 2014 (Day 44), the subject was hospitalized for pathological fracture in the left proximal femur (Grade 3). The femoral and pelvic images showed fracture in left proximal femur. No treatment information was provided. The study drug dose did not change. On 18 Jun 2014 (Day 59), the subject missed doses of the study drug due to insufficient quantity. On 19 Jun 2014 (Day 60), CT scan of pelvis showed sclerotin changes in the left proximal femur and the right hip bone and tumor response assessment showed disease progression. On 20 Jun 2014 (Day 61), the subject was withdrawn from the study due to disease progression and the subject received the last dose of study drug on 17 Jun 2014 (Day 58). The subject did not recover from the event. The Investigator considered pathological fracture in left proximal femur serious and not related to the study drug but related to disease progression.

On 18 Sep 2014 (Day 151, 93 days after the last dose), the subject died due to disease progression.

Subject Number	24161005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001254
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Blood bilirubin increased
AE(s) Leading to Discontinuation	Blood bilirubin increased

A 73-year-old Chinese male was diagnosed with hepatocellular carcinoma on 01 Aug 2014. Significant medical history included diabetes mellitus, hypertension, hepatic cirrhosis, liver biopsy, and cerebral infarction. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included karvea hct. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 23 Oct 2014 (Day 56), the subject experienced increased blood bilirubin (Grade 4) with total bilirubin 408.2 umol/L (NR: 1.7 – 18.8) and the study drug was withdrawn. On 24 Oct 2014 (Day 57), the subject was hospitalized for increased blood bilirubin. The subject received treatment but the details of treatment were unknown. The subject was withdrawn from study due to clinical disease progression and received the last dose of the study drug on 23 Oct 2014 (Day 56). The subject did not recover from increased blood bilirubin. The Investigator considered increased blood bilirubin serious and possibly related to the study drug and related to clinical disease progression.

On 02 Dec 2014 (Day 96, 40 days after the last dose), the subject died due to clinical disease progression. Autopsy was not performed.

Subject Number	24201007
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-002316
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Metastases to spine

A 38-year-old Chinese female was diagnosed with hepatocellular carcinoma on 04 Mar 2014. Significant medical history included gallbladder polyp, cholecystitis, gastritis, hepatitis B, splenomegaly, and pain (left waist pain). Previous anticancer therapies included other antineoplastic agents (TCM), hepatectomy, and regional chemotherapy (hepatic intra-arterial chemotherapy). Prior and concomitant medications included ambroxol, coptis chinensis, dexamethasone, diosmectite, heparinoid, ibandronic acid, metoclopramide, metoprolol, morphine, mosapride, nifedipine, oxycocet, oxycodone, and potassium. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of the liver; bilateral lung and lumbar spine masses. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 16 Oct 2014 (Day 1), treatment with study drug was initiated.

On 07 Dec 2014 (Day 53), the subject experienced metastases to spine (tumor compression due to spinal metastases; Grade 3) and was hospitalized. The subject also experienced urinary incontinence (Grade 3) and underwent a bladder catheterization. On 09 Dec 2014 (Day 55), CT scan showed T10, T12 – L2 vertebral bone destruction, uneven density, and showing soft tissue mass protruding into the spinal cord. On 09 Dec 2014 (Day 55), tumor response assessment showed disease progression, and the subject was withdrawn from the study, and received the last dose of the study drug on the same day (Day 55). The subject did not recover from metastases to spine and urinary incontinence. The Investigator considered the metastases to spine serious and not related to the study drug but related to disease progression; urinary incontinence nonserious and not related to the study drug but related to disease progression.

On 19 May 2015 (Day 216, 161 days after the last dose), the subject died due to disease progression.

Subject Number	30021001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001474
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Seizure
AE(s) Leading to Discontinuation	Seizure

A 47-year-old Asian male was diagnosed with hepatocellular carcinoma on 18 Dec 2012. Significant medical history included hepatitis B and hepatic cirrhosis. Previous anticancer therapies included investigational drug [PI-88 (sufonated monophosphorylated mannose oligosaccharides) subcutaneous injection], hepatectomy, and high frequency ablation. Prior and concomitant medications included acetylcysteine, calcium chloride, cefuroxime, cerol, cimetropium, dexamethasone, entecavir, famotidine, haloperidol, lansoprazole, levetiracetam, loperamide, lorazepam, metoclopramide, ranitidine, simeticone, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed bilateral lung masses. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 29 Oct 2013 (Day 22), the subject experienced palmar-plantar erythrodysesthesia syndrome (Grade 1). On 01 Feb 2014 (Day 117), the palmar-plantar erythrodysesthesia syndrome worsened to Grade 2 and the study drug dose was reduced to 400 mg/day due to this event. On 25 Mar 2014 (Day 169), the palmar-plantar erythrodysesthesia syndrome improved to Grade 1. On 24 Apr 2014 (Day 199), the subject recovered from palmar-plantar erythrodysesthesia syndrome. The Investigator considered palmar-plantar erythrodysesthesia syndrome nonserious and probably related to the study drug.

On 19 Apr 2014 (Day 194), the subject was hospitalized for seizure (Grade 2) described as generalized tonic-clonic seizure lasting for 2 to 3 minutes with right eyeball and head deviation. Head CT scan showed lesion on the right frontal lobe. Treatment included haloperidol, levetiracetam, lorazepam, and cerol and the study drug was withdrawn due to this event. The subject later on recovered from seizure on the same day. On 19 Apr 2014 (Day 194), tumor response assessment showed disease progression. On 21 Apr 2014 (Day 196), the subject was withdrawn from the study due to seizure secondary to disease progression and was discharged from hospital. The subject received the last dose of the study drug on 19 Apr 2014 (Day 194). The Investigator considered seizure serious and not related to study drug but related to disease progression.

On 30 Apr 2015 (Day 570, 376 days after the last dose), the subject died of unknown reason.

Subject Number	30031002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01363-CLI-KR
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Infection, Decreased appetite

A 55-year-old Asian male was diagnosed with hepatocellular carcinoma on 03 Jul 2013. Significant medical history included diabetes mellitus, gastritis, gastric erosion, hepatitis B, hypertension, and cancer pain. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included ambroxol, azor, cefixime, entecavir, fentanyl, glimepiride, hyoscine, insulin glulisine, isepamicin, metformin, metronidazole, myprodol, pronase, propacetamol, simeticone, sitagliptin, sulperazon, ultracet, and zipeprol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 30 Aug 2013 (Day 1), treatment with study drug was initiated.

On 31 Aug 2013 (Day 2), the subject was hospitalized due to unknown infection (Grade 3) and decreased appetite (Grade 2). On 03 Sep 2013 (Day 5), study drug was interrupted due to these events. The subject was treated with intravenous propacetamol, cefixime, sulperazon, isepamicin, and metronidazole. On 05 Sep 2013 (Day 7), the subject experienced cough (Grade 1) and productive cough with sputum (Grade 1). On 09 Sep 2013 (Day 11), the subject experienced chills (Grade 1). The subject was treated with ambroxol and zipeprol. On 12 Sep 2013 (Day 14), laboratory tests showed WBC 9.9 x10^9/L (NR: 4 – 10.8). The subject had chest x-ray, sputum culture, and urine culture (results were not provided). On 13 Sep 2013 (Day 15), the study drug was resumed at the same dose. On 15 Sep 2013 (Day 17), the subject recovered from chills, on 16 Sep 2013 (Day 18), recovered from infection and cough, on 17 Sep 2013 (Day 19), recovered from productive cough with sputum and on 10 Oct 2013 (Day 42), the subject recovered from decreased appetite. The Investigator considered infection and decreased appetite serious and possibly related to study drug; chills nonserious and possibly related to the study drug; cough and productive cough with sputum nonserious and not related to the study drug.

On 23 Oct 2013 (Day 55), tumor response assessment showed disease progression. On 26 Oct 2013 (Day 58), the study drug was interrupted due to disease progression. On 30 Oct 2013 (Day 62), the subject was withdrawn from study due to disease progression. The subject received the last dose of study drug on 25 Oct 2013 (Day 57).

On 12 Sep 2014 (Day 379, 322 days after the last dose), the subject died due to disease progression.

Subject Number	30041005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01477-CLI-KR
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Pyrexia

A 65-year-old Asian female was diagnosed with hepatocellular carcinoma on 01 Nov 2012. Significant medical history included hepatitis B, intervertebral disc protrusion, hypertension, bilateral knee arthroplasty, and osteoporosis. Previous anticancer therapies included hepatectomy (2x). Prior and concomitant medications included amlodipine, cefixime, chlorhexidine, clobetasol, filgrastim, ibandronic acid, lactulose, lekovit ca, loperamide, optiderm, other emollients and protectives (EV cream), paracetamol, propacetamol, and theobromine. At Screening, tumor assessments of target/non-target lesions via CT scan showed masses at bilateral lower and right upper lobes of lung. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 21 Mar 2014 (Day 1), treatment with study drug was initiated.

On 05 Apr 2014 (Day 16), the subject experienced diarrhea (Grade 3). On 06 Apr 2014 (Day 17), the subject experienced pyrexia (Grade 2) with a temperature of 39.5 ºC. On 07 Apr 2014 (Day 18), the subject was hospitalized for pyrexia (Grade 1) with body temperature of 38.6 ºC. On the same day (Day 18), the study drug was interrupted due to pyrexia and diarrhea. Laboratory tests showed absolute neutrophils count 1.714 x10^9/L (NR: not provided), WBC 2.8 x10^9/L (NR: 4 –10), and platelet count 52 x10^9/L (NR: 130 – 400). The subject was treated with cefixime, loperamide, paracetamol, chlorhexidine, and propacetamol. On 08 Apr 2014 (Day 19), the subject recovered from diarrhea. On 11 Apr 2014 (Day 22), the subject recovered from pyrexia. The Investigator considered pyrexia serious and possibly related to the study drug; diarrhea nonserious and possibly related to the study drug.

On 14 Apr 2014 (Day 25), the subject experienced decreased neutrophil count (Grade 3) with laboratory value of absolute neutrophils count 0.759 x10^9/L (NR: not provided). The study drug remained interrupted due to this event. On 25 Apr 2014 (Day 36), severity of decreased neutrophil count improved to Grade 2 with absolute neutrophils count 1.6 x10^9/L (NR: 1.7 – 7.9). On 29 Apr 2014 (Day 40), the subject recovered from decreased neutrophil count. On same day (Day 40), the study drug was resumed at a reduced dose of 400 mg/day due to this event. The Investigator considered decreased neutrophil count nonserious and possibly related to the study drug.

On 15 May 2014 (Day 56), the subject experienced decreased neutrophil count (Grade 2). On 28 May 2014 (Day 69), the event worsened to Grade 3 with absolute neutrophils count 0.885 x10^9/L (NR: not provided) and the subject was treated with filgrastim. On 29 May 2014 (Day 70), the study drug was interrupted due to decreased neutrophil count. On 11 Jun 2014 (Day 83), the study drug was resumed at same dose. On 13 Oct 2014 (Day 207), the subject recovered from decreased neutrophil count with absolute neutrophils count 1.71 x10^9/L

(NR: not provided). The Investigator considered decreased neutrophil count nonserious and possibly related to the study drug.

On 24 Oct 2014 (Day 218), tumor response assessment showed disease progression. On 27 Oct 2014 (Day 221), the subject was withdrawn from study due to disease progression and received the last dose of the study drug on the same day.

Subject Number	30051009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01563-CLI-KR
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Dyspnoea, Abdominal distension, Aspartate aminotransferase increased

A 46-year-old Asian male was diagnosed with hepatocellular carcinoma on 09 Apr 2014. Significant medical history included gastric ulcer and hepatitis B. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amino acids w/electrolytes/glucose, amoxicillin, ceftriaxone, clarithromycin, falkamin, furosemide, godex, human albumin, lansoprazole, medilac-s, megestrol, mg tna, multitrace-4, myprodol, oxyvit, pethidine, silybum marianum, spironolactone, tenofovir, tiropramide, tramadol, trimebutine, ursodeoxycholic acid, and vitamins (tamipool). At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver and multiple lung metastases. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 08 May 2014 (Day 1), treatment with study drug was initiated.

On 08 May 2014 (Day 1), the subject experienced increased aspartate aminotransferase (Grade 3). Laboratory tests showed AST 301 U/L (NR: 10 – 43). Treatment included silybum marianum and godex. The study dose was not changed. On 29 Aug 2014 (Day 114), the severity of increased aspartate aminotransferase worsened to Grade 4. Laboratory tests showed AST 867 U/L. The subject did not recover from increased aspartate aminotransferase. The Investigator considered increased aspartate aminotransferase serious (medically important event) and not related to study drug but related to disease progression.

On 16 Aug 2014 (Day 101), the subject experienced dyspnea (Grade 1) and abdominal distension (Grade 2). On 19 Aug 2014 (Day 104), the subject was hospitalized for dyspnea and abdominal distension. On the same day (Day 104), the subject experienced decreased appetite (Grade 3) which started as Grade 2 on 22 May 2014 (Day 15) and hypoalbuminemia (Grade 1). Laboratory tests showed albumin 30 g/L (NR: 33 – 53), ALT 132 U/L (NR: 5 – 46), AST 723 U/L (NR: 13 – 34), ALP 334 U/L (NR: 49 – 126), and total bilirubin 20.52 umol/L (NR: 8.55 – 30.78). CT scan of abdomen and pelvis showed increased amount of ascitic fluid with no demonstrable peritoneal seeding nodules; CT scan of chest showed increase in size and number of multiple metastatic nodules on bilateral lungs. On the same day (Day 104), tumor response assessment showed disease progression. Treatment included furosemide, spironolactone, amino acids w/electrolytes/glucose, multitrace-4, vitamins (tamipool), mg tna, human albumin, falkamin, ursodeoxycholic acid, and tiropramide. The study drug dose was not changed. The subject recovered from dyspnea on the same day (Day 104). On 21 Aug 2014 (Day 106), decreased appetite improved to Grade 2. On 22 Aug 2014 (Day 107), the subject was withdrawn from the study due to disease progression and received the last dose on 21 Aug 2014 (Day 106). On 30 Aug 2014 (Day 115), the subject experienced pyrexia (Grade 1). Treatment included ceftriaxone. On 03 Sep 2014 (Day 119), the subject recovered from pyrexia.

On 05 Sep 2014 (Day 121), the subject was discharged from the hospital. On 18 Sep 2014 (Day 134), the subject recovered from abdominal distension. The subject did not recover from decreased appetite and hypoalbuminemia. The Investigator considered dyspnea, abdominal distension serious and not related to the study drug; decreased appetite, pyrexia, and hypoalbuminemia nonserious and not related to the study drug.

On 26 Sep 2014 (Day 142, 36 days after the last dose), the subject died due to disease progression. It was unknown if autopsy was performed.

Subject Number	30051013
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003412
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Aspergillus infection

A 66-year-old Asian male was diagnosed with hepatocellular carcinoma on 27 Jun 2014. Significant medical history included alcoholic cirrhosis, hypertension, contrast media allergy (drug allergy of visipaque), and urge incontinence. Previous anticancer therapies included fluorouracil, radiotherapy to left lobe liver mass, and hepatic intra-arterial chemotherapy. Prior and concomitant medications included ambroxol acefyllinate, benproperine, carbocisteine, cefpodoxime, chlorphenamine, clobetasol, codeine, codenong, cough and cold preparations, diflucortolone, erdosteine, famotidine, fentanyl, furosemide, human albumin, hydrocortisone, lactulose, levodropropizine, lidocaine, megestrol, midazolam, moxifloxacin, mupirocin, piperacillin, potassium permanganate, prednisolone, propiverine, propofol, solifenacin, spironolactone, synatura, tamsulosin, targin, teprenone, tiropramide, tranexamic acid, ursodeoxycholic acid, and voriconazole. At Screening, tumor assessments of target/non-target lesions via CT scan showed lymphadenopathy at gastric region, lesions at quadrate and right liver lobes, and masses at bilateral lungs. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 28 Oct 2014 (Day 1), treatment with study drug was initiated.

On 09 Nov 2014 (Day 13), the subject experienced palmar-plantar erythrodysesthesia syndrome (Grade 3). Treatment included clobetasol, mupirocin, potassium permanganate, diflucortolone, and hydrocortisone. On 14 Nov 2014 (Day 18), the study drug was interrupted due to this event. On 25 Nov 2014 (Day 29), the severity of palmar-plantar erythrodysesthesia syndrome improved to Grade 2. On 27 Nov 2014 (Day 31), the study drug was resumed at a reduced dose of 600 mg/day due to palmar-plantar erythrodysesthesia syndrome. The subject did not recover from palmar-plantar erythrodysesthesia syndrome. The Investigator considered palmar-plantar erythrodysesthesia syndrome nonserious and possibly related to the study drug.

On 03 Jan 2015 (Day 68), the subject was hospitalized for aspergillus infection (Grade 3) with symptoms of cough (Grade 3) and productive cough (sputum production; Grade 3). Treatment included cefpodoxime, piperacillin, voriconazole, moxifloxacin, cough and cold preparations, benproperine, carbocisteine, codeine, erdosteine, synatura, tranexamic acid, codenong, ambroxol acefyllinate, levodropropizine, and prednisolone. On 22 Jan 2015 (Day 87), the study drug was interrupted due to aspergillus infection. On 22 Jan 2015 (Day 87), chest x-ray showed developed cavitary mass in right upper lobe fragment, newly developed consolidation in right lower lobe fragment, and no significant change of faint nodular opacities in left lower lobe fragment. On 23 Jan 2015 (Day 88), serum Aspergillus galactomannan Ag was positive. On 27 Jan 2015 (Day 92), the subject underwent bronchoscopy and lung biopsy which ruled out aspergillosis, pulmonary tuberculosis, and lung cancer. On 30 Jan 2015 (Day 95), the subject was discharged from the hospital. On 10 Feb 2015 (Day 106), the subject recovered from

cough and productive cough. The subject did not recover from aspergillus infection. The Investigator considered aspergillus infection serious and not related to the study drug; cough and productive cough nonserious and not related to the study drug.

On 09 Feb 2015 (Day 105), tumor response assessment showed disease progression. On 26 Feb 2015 (Day 122), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 21 Jan 2015 (Day 86).

On 07 Aug 2015 (Day 284, 198 days after the last dose), the subject died due to disease progression.

Subject Number	30051014
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003589
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Malignant pleural effusion

A 50-year-old Asian male was diagnosed with hepatocellular carcinoma on 10 Oct 2014. Significant medical history included chronic gastritis, upper abdominal pain, erosive gastritis, hepatitis B, hepatic cirrhosis, and musculoskeletal pain (shoulder). The subject did not receive any previous anticancer therapies. Prior and concomitant medications included acetylcysteine, amino acids w/electrolytes, amino acids w/electrolytes/glucose, amlodipine, ascorbic acid w/biotin/calcium/carbohydrate, azelastine, benproperine, carbocisteine, carnitine hydrochloride w/cyanocoba, carol-f, celecoxib, chlorphenamine, dexamethasone, diazepam, falkamin, fentanyl, furosemide, general nutrients, hetastarch, hyoscine, human albumin, lamivudine, megestrol, metoclopramide, multitrace-4, myprodol, ondansetron, oxycodone, propofol, ramosetron, targin, tramadol, and vitamins. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, pelvis and lumbar lesion, and para-aortic lymphadenopathy. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 28 Oct 2014 (Day 1), treatment with study drug was initiated.

On 25 Jan 2015 (Day 90), the subject experienced malignant pleural effusion (Grade 3) and was hospitalized on 29 Jan 2015 (Day 94) for further evaluation. On 01 Feb 2015 (Day 97), CT scan of chest showed newly developed large amount of loculated left pleural effusion with diffuse pleural thickening and nodules and enhancement including mediastinal pleura suggestive of malignant effusion with pleural metastasis. The subject underwent percutaneous catheter drainage and insertion of implantable pleural catheter and was also treated with furosemide. On 01 Feb 2015 (Day 97), tumor response assessment showed disease progression. On 02 Feb 2015 (Day 98), the study drug was interrupted due to malignant pleural effusion. The subject did not recover from malignant pleural effusion. The Investigator considered malignant pleural effusion serious and not related to the study drug but related to disease progression.

On 12 Feb 2015 (Day 108), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 01 Feb 2015 (Day 97). On 17 Feb 2015 (Day 113), tumor response assessment confirmed disease progression.

On 22 Mar 2015 (Day 146, 49 days after the last dose), the subject died due to disease progression.

Subject Number	30061001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01362-CLI-KR
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Metastases to bone, Ascites

A 47-year-old Asian male was diagnosed with hepatocellular carcinoma on 20 Jul 2012. Significant medical history included chronic hepatitis B, general pain, and hepatic cirrhosis. Previous anticancer therapies included transcatheter arterial chemoembolization, transarterial radioembolization, and radiotherapy to spine-cervical 7, thoracic 4, thoracic 8, and lumbar 4. Prior and concomitant medications included amlodipine, azelastine, cefotaxime, cefpodoxime, clobetasol, de shuang, ebastine, fentanyl, fexofenadine, furosemide, glucose, hepatamine, human albumin, lactulose, magnesium oxide, megestrol, oxycodone, pethidine, propacetamol, simeticone, sodium chloride, spironolactone, telbivudine, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at caudate lobe and quadrate lobe of liver; and right pelvic mass. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 02 Jul 2013 (Day 1), treatment with study drug was initiated.

On 04 Jul 2013 (Day 3), the subject experienced urticaria (Grade 2). On 05 Jul 2013 (Day 4), the study drug was reduced to 400 mg/day due to this event. Treatment included ebastine, fexofenadine, azelastine, and clobetasol. On 07 Jul 2013 (Day 6), the study drug was interrupted due to urticaria. On 15 Jul 2013 (Day 14), the subject recovered from urticaria. On 16 Jul 2013 (Day 15), the study drug was resumed at same dose. The Investigator considered urticaria nonserious and probably related to study drug.

On 10 Sep 2013 (Day 71), tumor response assessment showed disease progression. On the same day (Day 71), the subject was hospitalized for metastases to bone (skull metastases; Grade 2). Treatment included radiotherapy to brain. On 12 Sep 2013 (Day 73), the study drug was interrupted due to this event. The subject was discharged from the hospital. On 13 Sep 2013 (Day 74), the subject experienced hypoalbuminemia (Grade 2) with albumin 29 g/L (NR: 35 – 55) and was treated with human albumin. On the same day (Day 74), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on 11 Sep 2013 (Day 72). The subject did not recover from metastases to bone and hypoalbuminemia. The Investigator considered metastases to bone serious and not related to study drug but related to disease progression; hypoalbuminemia nonserious and not related to study drug.

On 23 Sep 2013 (Day 84), the subject was hospitalized for ascites (Grade 2). On the same day (Day 84), the subject experienced hyperbilirubinemia (Grade 2). Laboratory tests showed total bilirubin 31.806 umol/L (NR: 1.71- 20.52) and AST 101 U/L (NR: 10 – 40). Treatment included furosemide, spironolactone, propacetamol, cefotaxime, cefpodoxime, and hepatamine. On 01 Oct 2013 (Day 92), the subject was discharged from the hospital. The subject did not

recover from ascites and hyperbilirubinemia. The Investigator considered ascites serious and not related to study drug; hyperbilirubinemia nonserious and not related to study drug.

On 13 Oct 2013 (Day 104, 32 days after the last dose), the subject died due to disease progression. It is unknown if an autopsy was performed.

Subject Number	30061006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-002842
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Ascites (2x)
AE(s) Leading to Discontinuation	Ascites

A 73-year-old Asian male was diagnosed with hepatocellular carcinoma on 11 May 2012. Significant medical history included hepatic cyst, renal cyst, chronic gastritis, chronic hepatitis B, diabetes mellitus, duodenal ulcer, and hepatic cirrhosis. Previous anticancer therapies included high frequency ablation and transcatheter arterial chemoembolization. Prior and concomitant medications included acetylcysteine, alprazolam, ambroxol, amino acids, amlodipine, amoxicillin, bepotastine, calcium acetate, calcium polystyrene sulfonate, cefotaxime, chlorhexidine, chlorphenamine, chlorpromazine, cimetropium, ciprofloxacin, codeine, corydalis yanhusuo tuber w/ipomoea nil seed, cough and cold preparations (cough syrup), daivobet, entecavir, erdosteine, falkamin, fentanyl, festal plus, flumazenil, furosemide, fusidic acid, glucose, hepatamine, human albumin, insulin glargine, insulin lispro, lactobacillus acidophilus, lactulose, lidocaine, magnesium oxide, megestrol, menadione, meropenem, metoclopramide, midazolam, morphine, nafamostat, ornithine, oxycodone, pantoprazole, pethidine, potassium, pronase, propacetamol, pseudoephedrine, quetiapine, ranitidine, rebamipide, simeticone, smoflipid, sodium bicarbonate, spironolactone, teicoplanin, terlipressin, thiamine, tiropramide, torasemide, urea, ursodeoxycholic acid, vitamin k, and vitamins. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at left, right, and quadrate lobes of liver; CT scan showed bilateral lung masses. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 22 May 2014 (Day 1), treatment with study drug was initiated.

On 28 Dec 2014 (Day 221), the subject was hospitalized for ascites (Grade 3) and the study drug was interrupted due to this event. The subject underwent paracentesis and was also treated with furosemide, spironolactone, and human albumin. On 02 Jan 2015 (Day 226), peritoneal fluid analysis showed no evidence of malignancy, many histiocytes, few neutrophils, and lymphocytes. On 08 Jan 2015 (Day 232), the study drug was resumed at same dose. On 13 Jan 2015 (Day 237), the subject recovered from ascites. The Investigator considered ascites serious and not related to the study drug.

On 21 Apr 2015 (Day 335), the subject was hospitalized for a recurrence of ascites (Grade 3). The subject underwent abdominal cavity drainage (multiple times) and was also treated with furosemide, human albumin, and torasemide. On 27 Apr 2015 (Day 341), the study drug was interrupted due to ascites. On 01 May 2015 (Day 345), the study drug was resumed at the same dose. On 02 Jun 2015 (Day 377), the study drug was interrupted due to ongoing ascites. The Investigator considered ascites serious and not related to the study drug.

On 02 Jun 2015 (Day 377), the subject experienced increased blood creatinine (Grade 1). On 27 Jul 2015 (Day 432), the subject experienced increased blood bilirubin (Grade 2). On 08 Aug 2015 (Day 444), the subject experienced decreased urine output (Grade 3), and increased blood bilirubin worsened to Grade 3. See table below. On 09 Aug 2015 (Day 445), the subject experienced decreased appetite (Grade 2), hypotension (Grade 1), and increased blood creatinine worsened to Grade 3. On 10 Aug 2015 (Day 446), the subject was hospitalized for bacterial peritonitis (spontaneous bacterial peritonitis; Grade 3) and hepatorenal syndrome (Grade 4). Peritoneal fluid analysis confirmed spontaneous bacterial peritonitis. On the same day (Day 446), the subject recovered from hypotension. On 11 Aug 2015 (Day 447), the subject experienced anemia (Grade 3). Treatment included renal replacement therapy, terlipressin, ciprofloxacin, smoflipid, hepatamine, teicoplanin, amino acids, ornithine, and blood transfusion. On 16 Aug 2015 (Day 452), the subject recovered from increased blood bilirubin. On 24 Aug 2015 (Day 460), the subject was withdrawn from the study due to persistent ascites and received the last dose of the study drug on 01 Jun 2015 (Day 376). On 25 Aug 2015 (Day 461), the subject recovered from increased blood creatinine. On 26 Aug 2015 (Day 462), repeat CT scan of abdomen and pelvis showed ascites. On 27 Aug 2015 (Day 463), tumor response assessment showed disease progression. On 28 Sep 2015 (Day 495, 119 days after the last dose), the subject died due to hepatorenal syndrome. At the time of death, the subject had not recovered from bacterial peritonitis, decreased appetite, anemia, decreased urine output, and ascites. The Investigator considered hepatorenal syndrome, bacterial peritonitis, and ascites serious and not related to the study drug; decreased appetite, anemia, decreased urine output, hypotension, increased blood bilirubin, and increased blood creatinine nonserious and not related to the study drug.