from fatigue and asthenia. The subject received the last dose of the study drug on 11 May 2014 (Day 143). The Investigator considered malignant neoplasm progression serious and not related to the study drug but related to disease progression; fatigue nonserious and not related to the study drug but related to disease progression; asthenia nonserious and not related to the study drug.

Subject Number	16031019
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-005779
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Ascites
Non-Fatal SAE(s)	Oedema peripheral, General physical health deterioration, Fatigue, Ascites
AE(s) Leading to Discontinuation	Fatigue, Ascites
Death due to PD	Yes

A 54-year-old white male was diagnosed with hepatocellular carcinoma on 17 Nov 2014. Significant medical history included gastritis, erosive gastritis, hypertension, hypothyroidism, impaired fasting glucose, upper abdominal pain (pain of the right hypochondrium), thyroidectomy, and transient ischemic attack. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included akritoin, electrolytes, enoxaparin, furosemide, levothyroxine, metoprolol, nifuroxazide, sodium chloride, spironolactone, telmisartan, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at segment 6 and 8 (sub-diaphragmatic); masses at left lingular, right lower lobe lung and omentum; para-caval, right hilar, porta-hepatis, right mediastinal and below carina lymphadenopathies, and multiple bilateral lung metastases. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 08 Jan 2015 (Day 1), treatment with study drug was initiated.

On 07 Apr 2015 (Day 90), the subject was hospitalized for peripheral edema (Grade 3) and general physical health deterioration (Grade 3). The subject was treated with spironolactone, electrolytes, nifuroxazide, and furosemide. The study drug dose was not changed. On 13 Apr 2015 (Day 96), the subject recovered from these events. The Investigator considered peripheral edema and general physical health deterioration serious and not related to the study drug.

On 16 Apr 2015 (Day 99), tumor response assessment showed disease progression.

On 17 Apr 2015 (Day 100), the subject was hospitalized for fatigue (Grade 3) and worsening of ascites (unknown ascites; Grade 3) which started as Grade 1 on 05 Feb 2015 (Day 29). Laboratory tests showed AST 272 U/L (NR: 0 – 50), ALT 84 U/L (NR: 0 – 50), ALP 634 U/L (NR: 30 – 120), total bilirubin 27.3 umol/L (NR: 5 – 21), albumin 25.7 g/L (NR: 35 – 52), LDH 803 U/L (NR: 0 – 247), creatinine 130.832 umol/L (NR: 59.228 – 103.428). The subject underwent paracentesis and was also treated with tramadol, spironolactone, and furosemide. On 21 Apr 2015 (Day 104), the subject was withdrawn from study drug due to ascites and fatigue and on the same day (Day 104), received last dose of the study drug. The subject was discharged from the hospital by request of his wife. On 29 Apr 2015 (Day 112, 8 days after the last dose), the subject died due to ascites secondary to disease progression. Autopsy was not

performed. At the time of death, the subject had not recovered from fatigue. The Investigator considered ascites and fatigue serious and not related to study drug, but related to disease progression.

Subject Number	19021004
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-006062
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Ischaemic stroke
Non-Fatal SAE(s)	Ischaemic stroke
AE(s) Leading to Discontinuation	Ischaemic stroke
Death due to PD	No

A 67-year-old white male was diagnosed with hepatocellular carcinoma on 29 Aug 2013. Significant medical history included atrial fibrillation, chronic cholecystitis, type 2 diabetes mellitus, essential hypertension, myocardial ischemia, obesity, and splenomegaly. Previous anticancer therapies included hepatectomy (right lobe) and high frequency ablation. Prior and concomitant medications included ademetionine, loperamide, and omeprazole. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right and left liver lobes. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

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

On 05 Mar 2015 (Day 365), the subject experienced electrocardiogram QT prolonged (Grade 1) with QTcF 483 msec (NR: <430). Laboratory tests showed INR 1.3 (NR: 0.9 – 1.1) and PT 14.4 sec (NR: 9.4 – 12.5). On 06 Mar 2015 (Day 366), the subject was hospitalized for ischemic stroke (Grade 4). The subject was treated with unspecified medications and the study drug was withdrawn. On 30 Mar 2015 (Day 390, 25 days after the last dose), the subject died due to ischemic stroke. Autopsy showed ischemic stroke and cerebral edema as the cause of death. The subject received the last dose of the study drug on 05 Mar 2015 (Day 365). At the time of death, the subject had not recovered from electrocardiogram QT prolonged. The Investigator considered ischemic stroke serious and possibly related to the study drug; electrocardiogram QT prolonged nonserious and possibly related to the study drug.

Subject Number	19021031
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-010694
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Sudden death
AE(s) Leading to Discontinuation	Sudden death
Death due to PD	Unknown

A 66-year-old white male was diagnosed with hepatocellular carcinoma on 28 May 2015. Significant medical history included angina pectoris, chronic cholecystitis, chronic gastroduodenitis, chronic pancreatitis, type 2 diabetes mellitus, esophageal varices, hepatic cirrhosis, hypertension, and coronary arterial stent insertion. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included fosinopril, glibomet, and indapamide. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left lobe of liver, multiple liver lesions, porta-hepatis lymphadenopathy, and bilateral lung mass. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 03 Jun 2015 (Day 1), treatment with study drug was initiated.

On 05 Sep 2015 (Day 95), the daughter reported that the subject had a sudden death (cause was unknown). It was unknown if an autopsy was performed. The subject received the last dose of study drug on the same day (Day 95). The Investigator considered this event serious and not related to study drug.

Subject Number	24021011
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000492
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Upper gastrointestinal haemorrhage
Non-Fatal SAE(s)	Upper gastrointestinal haemorrhage (2x), Shock
AE(s) Leading to Discontinuation	Shock, Upper gastrointestinal haemorrhage
Death due to PD	No

A 52-year-old Chinese male was diagnosed with hepatocellular carcinoma on 10 Sep 2014. Significant medical history included hepatic cirrhosis, gastritis erosive, esophageal varices, gastric varices, hepatitis B, hepatic cyst, ascites, and right upper abdominal pain. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amino acids, bucinnazine, ceftezole, codeine, fats (medium/long chain fat milk), glutathione, glycyrrhizic acid, granisetron, hemocoagulase, hetastarch, human albumin, morphine, norepinephrine, octreotide, omeprazole, oxycocet, piton (pituitrin), potassium, proliv, thrombin, torasemide, and tropisetron. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right and left lobes of liver and bilateral pulmonary masses. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 18 Sep 2014 (Day 1), treatment with study drug was initiated.

On 30 Sep 2014 (Day 13), the subject experienced nausea (Grade 1) and vomiting (Grade 1) and was hospitalized for upper gastrointestinal hemorrhage (Grade 4). The study drug was interrupted due to upper gastrointestinal hemorrhage. On the same day (Day 13), the subject also had acute upper respiratory tract infection (Grade 3), anemia (Grade 1), oropharyngeal pain (Grade 1), pyrexia (Grade 1), prolonged prothrombin time (Grade 1) and increased international normalized ratio (Grade 1). Laboratory tests showed RBC 3.87 x10^12/L (NR: 4 – 5.6), Hgb 119 g/L (NR: 125 – 170), Hct 0.362 L/L (NR: 0.37 – 0.51), PT 15.4 sec (NR: 9 – 12.8), INR 1.44 (NR: 0.8 – 1.2), and positive occult blood in vomit and stool test. The subject was treated with hemocoagulase, octreotide, piton, omeprazole, tropisetron and norepinephrine. The subject recovered from pyrexia, nausea, vomiting, and oropharyngeal pain on 01 Oct 2014 (Day 14); and recovered from upper gastrointestinal hemorrhage on 08 Oct 2014 (Day 21). On 09 Oct 2014 (Day 22), the study drug was resumed at a reduced dose of 400 mg/day due to upper gastrointestinal hemorrhage. The subject did not recover from acute respiratory infection, prolonged prothrombin time, increased international normalized ratio, and anemia. On 21 Oct 2014 (Day 34), the subject was discharged from hospital. The Investigator considered upper gastrointestinal hemorrhage serious and possibly related to study drug; vomiting, nausea, anemia, oropharyngeal pain, pyrexia, prolonged prothrombin time, increased international normalized ratio, and acute respiratory tract infection nonserious and not related to study drug.

On 10 Nov 2014 (Day 54), the subject experienced shock (Grade 4), dizziness (Grade 3), nausea (Grade 1), and vomiting (Grade 1). On 11 Nov 2014 (Day 55), the subject experienced upper

abdominal pain (Grade 3), increased blood potassium (Grade 3) and was hospitalized with a diagnosis of upper gastrointestinal hemorrhage (Grade 4). The subject also experienced anemia (Grade 2). Vitals signs showed blood pressure of 80/50 mmHg, heart rate of 114 bpm and respiratory rate of 26 breaths/min. Laboratory tests showed RBC 2.52 x10^12/L, Hgb 77 g/L, Hct 0.235 L/L, potassium 5.7 mmol/L (NR: 3.5 – 5), and negative occult blood in vomit. The subject was treated with hetastarch, morphine, omeprazole, granisetron, octreotide, hemocoagulase, thrombin, morphine, and piton. Later that day (Day 55, 1 day after the last dose), the subject died due to worsening upper gastrointestinal hemorrhage. The subject received the last dose of the study drug on 10 Nov 2014 (Day 54). Autopsy was not performed. At the time of death, the subject had not recovered from shock, nausea, upper abdominal pain, vomiting, dizziness, increased blood potassium, and anemia. The Investigator considered shock, upper gastrointestinal hemorrhage serious and not related to study drug; nausea, vomiting, dizziness, increased blood potassium, and anemia nonserious and not related to study drug.

Subject Number	24031002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01518-CLI-CN
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Oesophageal varices haemorrhage
Non-Fatal SAE(s)	Diplegia
Death due to PD	Yes

A 56-year-old Chinese male was diagnosed with hepatocellular carcinoma in Oct 2013. Significant medical history included abdominal pain, back pain, decreased appetite, hepatic cirrhosis, hepatitis B, malaise, and bone pain (right humeral). Previous anticancer therapies included transcatheter arterial chemoembolization and unspecified herbal and traditional medicine (aidi injection chinese traditional medication). Prior and concomitant medications included fats (emulsion injection), glucose injection, glutathione, glycyrrhizic acid, morphine, polyene phosphatidylcholine, and thymopentin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left liver lobe; left and right mediastinal and retroperitoneal lymphadenopathies; bilateral lower lobes lung masses and multiple lung metastases; and inferior vena cava tumor thrombus. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 20 May 2014 (Day 40), the subject experienced oral neoplasm (gingival neoplasm; Grade 2). The subject refused any testing or treatment. The study drug dose was not changed. The subject did not recover from oral neoplasm. The Investigator considered oral neoplasm nonserious and not related to the study drug.

On 30 May 2014 (Day 50), the subject slipped and fell and was hospitalized for diplegia (paralysis of both lower limbs; Grade 4) and refused diagnostic testing. The subject was treated with nutritional and symptomatic support. On 03 Jun 2014 (Day 54), the subject was withdrawn from the study due to subject's choice and received the last dose of the study drug on the same day. No imaging test was done to confirm clinical disease progression. The subject did not recover from diplegia. The Investigator considered diplegia serious and not related to study drug.

On 17 Jun 2014 (Day 68), the subject vomited coffee-colored liquid due to esophageal varices hemorrhage and refused further treatment. On the same day (Day 68, 14 days after the last dose), the subject died due to esophageal varices hemorrhage. Autopsy was not performed. The Investigator considered esophageal varices hemorrhage serious and not related to study drug but related to disease progression.

Subject Number	24031009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-002062
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Respiratory failure
AE(s) leading to Discontinuation	Respiratory failure
Death due to PD	Yes

A 36-year-old Chinese male was diagnosed with hepatocellular carcinoma on 10 Jun 2014. Significant medical history included hepatitis B and hepatic cirrhosis. Previous anticancer therapy included hepatectomy. No prior or concomitant medications were reported. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right and left lobes of the liver, retroperitoneal lymphadenopathy, multiple lung metastases, left upper lobe lung mass, and metastatic tumor of pleura. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 27 Nov 2014 (Day 43), the subject died at home and the cause of death was respiratory failure secondary to clinical disease progression. The subject received the last dose of the study drug on the same day (Day 43). Autopsy was not performed and no imaging tests to confirm disease progression. The Investigator considered respiratory failure serious and not related to the study drug.

Subject Number	24041013
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001691
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Respiratory failure
AE(s) Leading to Discontinuation	Respiratory failure
Death due to PD	Unknown

A 54-year-old Chinese female was diagnosed with hepatocellular carcinoma in Jan 2013. Significant medical history included arachnoid cyst, diabetes mellitus, hysterectomy, postoperative endometrial carcinoma, postoperative feet cyst, hepatitis B, left maxillary sinusitis, pelvic effusion, pericardial effusion, pleural effusion, pneumonia, post hysterectomy, pyoperitoneum, and postoperative thyroid neoplasm. Previous anticancer therapies included radiotherapy to mass in right lobe of liver and right kidney, hepatic intra-arterial chemotherapy, and radiofrequency ablation. Prior and concomitant medications included adefovir, aminophylline, anisodamine, calcium w/vitamin D, entecavir, furosemide, glucose, heparin, insulin aspart, insulin detemir, omeprazole, oxygen, platycodon grandiflorus, polyene phosphatidylcholine, and ringer-lactate. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver; masses at right breast, right kidney, right rib, and bilateral lungs; lymphadenopathy at bilateral hilar areas, mediastinum, and right angle of the heart. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 18 Oct 2014 (Day 1), treatment with study drug was initiated.

On 30 Oct 2014 (Day 13), the subject experienced increased blood bilirubin (Grade 2), increased gamma-glutamyltransferase (Grade 3), increased blood lactate dehydrogenase (Grade 2), asthenia (Grade 3), increased C-reactive protein (Grade 2), and increased aspartate aminotransferase (Grade 1). Laboratory tests showed total bilirubin 53.9 umol/L (NR: 1.7 – 18.8), AST 97 U/L (NR: 10 – 36), CRP 258.7 mg/L (NR: 0 – 5), and GGT 404 U/L (NR: 5 – 32). On 12 Nov 2014 (Day 26), the subject experienced liver tumor rupture (Grade 2) and decreased appetite (Grade 2). On 13 Nov 2014 (Day 27), the severity of increased blood bilirubin, liver tumor rupture, and increased aspartate aminotransferase worsened to Grade 3. On same day (Day 27), the subject experienced prolonged prothrombin time (Grade 2) and hypovolemic shock (Grade 3). On 14 Nov 2014 (Day 28), the subject was hospitalized with symptoms of shortness of breath, epigastric tenderness, and weak bowel sounds. The subject was diagnosed with respiratory failure, advanced HCC liver lesion near lung capsule, intra hepatic vessels with thrombosis, and liver tumor rupture and bleeding with shedding of thrombosis. Laboratory tests showed AST 200 U/L, ALP 164 U/L (NR: 30 – 115), GGT 449 U/L, creatinine 53 umol/L (NR: 62 – 124), PT 16.8 sec (NR: 9.4 – 12.5), AFP >72604.1 ug/L (NR: 0 – 6.1), and total bilirubin 81.1 umol/L. The subject was treated with ringer-lactate, glucose, furosemide, oxygen, omeprazole, aminophylline, and anisodamine. On 14 Nov 2014 (Day 28, 1 day after the last dose), the subject died due to respiratory failure.

The subject received the last dose of study drug on 13 Nov 2014 (Day 27). At the time of death, the subject had not recovered from increased blood bilirubin, increased gamma-glutamyltransferase, asthenia, increased blood lactate dehydrogenase, increased C-reactive protein, increased aspartate aminotransferase, tumor rupture, decreased appetite, hypovolemic shock, and prolonged prothrombin time. Autopsy was not performed. The Investigator considered respiratory failure serious and possibly related to study drug; all other events nonserious and possibly related to study drug.

Subject Number	24071005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-002213
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Non-Fatal SAE(s)	Abdominal pain, Jaundice, Coma hepatic
AE(s) Leading to Discontinuation	Abdominal pain, Jaundice
Death due to PD	Yes

A 75-year-old Chinese male was diagnosed with hepatocellular carcinoma on 12 Sep 2000. Significant medical history included chronic cholecystitis, duodenitis, erosive gastritis, hepatitis B, and hypertension. Previous anticancer therapies included hepatectomy, hepatic intra-arterial chemotherapy, radiofrequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included amlodipine, esomeprazole, fosinopril, and hydrotalcite. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right and left lobes of liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 6.

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

On 06 Nov 2014 (Day 2), the subject was hospitalized for abdominal pain (Grade 3) and jaundice (Grade 3). Laboratory tests showed total bilirubin 76.3 umol/L (NR: not provided), ALT 80 U/L (NR: not provided), AST 214 U/L (NR: not provided), and ALP 423 U/L (NR: not provided). Treatment was given but specific medications were not provided. On 13 Nov 2014 (Day 9), the subject experienced hepatic coma (Grade 4). On 14 Nov 2014 (Day 10), the study drug was withdrawn due to abdominal pain and jaundice and on 17 Nov 2014 (Day 13), the subject was withdrawn from study due to clinical disease progression. The subject received the last dose of study drug on 13 Nov 2014 (Day 9). On 17 Nov 2014 (Day 13, 4 days after the last dose), the subject died due to malignant neoplasm progression. At the time of death, the subject had not recovered from hepatic coma, abdominal pain, and jaundice. Autopsy was not performed. The Investigator considered malignant neoplasm progression, abdominal pain, hepatic coma, and jaundice serious and not related to study drug but related to disease progression.

Subject Number	24101011
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-017543
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 68-year-old Chinese male was diagnosed with hepatocellular carcinoma on 06 Mar 2014. Significant medical history included hepatitis B. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included bicyclol and omeprazole. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left lobe of liver, left lingular, and left lower lobe of lung. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 23 Oct 2014 (Day 43), the subject experienced fatigue (Grade 1) and liver injury (Grade 1). Laboratory tests showed albumin 31 g/L (NR: 35 – 55), ALP 245 U/L (NR: 43 – 115), ALT 401 U/L (NR: 10 – 40), AST 616 U/L (NR: 10 – 43), total bilirubin 46.9 umol/L (NR: 1.7 – 18.8), and GGT 145 U/L (NR: 10 – 49). On 26 Oct 2014 (Day 46), the subject experienced dysphonia (Grade 1). The study drug dose did not change. The subject did not recover from these events. The Investigator considered fatigue and liver injury nonserious and possibly related to the study drug.

On 06 Nov 2014 (Day 57), tumor response assessment showed disease progression. On 10 Nov 2014 (Day 61), the subject was withdrawn from study due to disease progression and received the last dose of the study drug on 07 Nov 2014 (Day 58).

On 02 Dec 2014 (Day 83, 25 days after the last dose), the subject died due to malignant neoplasm progression. It was unknown if an autopsy was performed. The Investigator considered this event serious and not related to the study drug.

Subject Number	24111007
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000928
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Renal impairment
Non-Fatal SAE(s)	Jaundice cholestatic, Renal impairment
AE(s) Leading to Discontinuation	Jaundice cholestatic
Death due to PD	Yes

A 41-year-old Chinese male was diagnosed with hepatocellular carcinoma on 24 Oct 2013. Significant medical history included abdominal pain, hepatitis B, and hepatic cirrhosis. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included alanyl glutamine, amino acids, bucinnazine, esomeprazole, glucose injection, glycyrrhizic acid, oxycocet, oxycodone, promethazine, and retinol w/tocopherol/vitamin D/vitamin K. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver; para-aortic and porta-hepatis lymphadenopathies, and mass at left lower lobe of lung. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 28 Jul 2014 (Day –3), the subject experienced abdominal pain (Grade 2) and was treated with oxycodone, bucinnazine, and promethazine. The subject did not recover from this event. The Investigator considered this event nonserious and not related to study drug.

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

On 30 Sep 2014 (Day 62), the subject was hospitalized for cholestatic jaundice (Grade 4). Laboratory tests showed ALT 159 U/L (NR: not provided), AST 317 U/L (NR: not provided), ALP 1481 U/L (NR: not provided), and total bilirubin 253.7 umol/L (NR: not provided). Abdominal ultrasound showed pleural effusion and ascites. Treatment included glycyrrhizic acid. On 11 Oct 2014 (Day 73), the study drug was interrupted due to cholestatic jaundice. On 15 Oct 2014 (Day 77), the subject underwent biliary drainage. Laboratory tests showed AST 277 U/L (NR: 15 – 40), ALT 175 U/L (NR: 9 – 50), ALP 2231 U/L (NR: 45 – 125), and total bilirubin 296.4 umol/L (NR: 3.4 – 20.5). On 20 Oct 2014 (Day 82), the study drug was withdrawn due to cholestatic jaundice secondary to clinical disease progression and the subject received the last dose of study drug on 10 Oct 2014 (Day 72). The subject was discharged from the hospital on 21 Oct 2014 (Day 83). The subject did not recover from cholestatic jaundice. The Investigator considered cholestatic jaundice serious and not related to study drug but related to disease progression.

On 01 Nov 2014 (Day 94), the subject experienced renal impairment (Grade 4) with urine output of 500 to 600 ml after diuretics. Renal function tests and treatments were not provided. On 07 Nov 2014 (Day 100, 28 days after the last dose), the subject died due to renal impairment

secondary to clinical disease progression. The Investigator considered renal impairment serious and not related to study drug but related to disease progression.

Subject Number	24111045
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-005677
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Upper gastrointestinal haemorrhage
Non-Fatal SAE(s)	Basal ganglia haemorrhage
Death due to PD	Yes

A 66-year-old Chinese male was diagnosed with hepatocellular carcinoma on 14 Jan 2015. Significant medical history included hepatic cirrhosis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included ademetionine, alanyl glutamine, amlodipine, deproteinized calf blood injection, coenzyme complex, edaravone, glycyrrhizic acid, hydrochlorothiazide, neurobion, nicergoline, oxycocet, pantoprazole, trimebutine, and unspecified herbal and traditional medicine (xingnaojing). At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of liver and right branch of portal vein of liver. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 06 Feb 2015 (Day 1), treatment with study drug was initiated.

On 31 Mar 2015 (Day 54), the subject experienced unconsciousness for three minutes and had a right side body weakness. On 02 Apr 2015 (Day 56), the blood pressure was 119/76 mmHg. Computerized tomogram of head showed high density left basal ganglia hemorrhage. The subject was diagnosed with basal ganglia hemorrhage (Grade 4) and the study drug was interrupted due to this event. On 03 Apr 2015 (Day 57), the subject was admitted for basal ganglia hemorrhage. The subject did not take any concomitant anti-coagulant medications. The subject was treated with nicergoline, edaravone, and xingnaojing. On 08 Apr 2015 (Day 62), the subject recovered from basal ganglia hemorrhage and was discharged from the hospital. On 14 Apr 2015 (Day 68), the study drug was resumed at same dose. The Investigator considered basal ganglia hemorrhage serious and possibly related to the study drug.

On 19 Aug 2015 (Day 195), the subject experienced decreased weight (Grade 3) with body weight of 46 kg (Baseline: 60 kg) which started on 05 Mar 2015 (Day 28) as Grade 1 with body weight of 56.5 kg. On the same day (Day 195), the subject experienced increased aspartate aminotransferase (Grade 3) and increased alanine aminotransferase (Grade 3). Laboratory tests showed total bilirubin 8.4 umol/L (NR: 0 – 18.8), albumin 34 g/L (NR: 35 – 55), ALP 250 U/L (NR: 43 – 115), ALT 264 U/L (NR: 10 – 40), AST 560 U/L (NR: 10 – 43), CRP 107 mg/L (NR: 0 – 5), and GGT 332 U/L (NR: 10 – 49). The study drug dose was not changed. On 21 Aug 2015 (Day 197), the subject experienced ascites (Grade 1). On 17 Sep 2015 (Day 224), the subject experienced increased blood bilirubin (Grade 3) with total bilirubin 51.6 umol/L, increased blood alkaline phosphatase (Grade 3) with ALP 633 U/L, and the severity of increased aspartate aminotransferase worsened to Grade 4 with AST 882 U/L. The subject was treated with ademetionine and glycyrrhizic acid. On the same day (Day 224),

tumor response assessment showed disease progression. On 18 Sep 2015 (Day 225), the study drug was interrupted as per Investigator's decision. On 21 Sep 2015 (Day 228), the subject was withdrawn from study due to disease progression and received the last dose of the study drug on 17 Sep 2015 (Day 224). The subject did not recover from decreased weight, increased blood bilirubin, increased aspartate aminotransferase, increased alanine aminotransferase, increased blood alkaline phosphatase, and ascites. The Investigator considered decreased weight, increased blood bilirubin, increased aspartate aminotransferase, increased alanine aminotransferase, increased blood alkaline phosphatase, and ascites nonserious and not related to the study drug.

On 03 Oct 2015 (Day 240, 16 days after the last dose), the subject died due to upper gastrointestinal hemorrhage secondary to disease progression. Autopsy was not performed. No additional information is available. The Investigator considered upper gastrointestinal hemorrhage serious and not related to the study drug but related to disease progression.

Subject Number	24131031
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-017809
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 59-year-old Chinese male was diagnosed with hepatocellular carcinoma in Oct 2013. Significant medical history included hepatic cyst and hepatitis B. Previous anticancer therapies included transcatheter arterial chemoembolization and hepatectomy. Prior and concomitant medications included aluminum phosphate, amino acids, bacillus lichenformis, bicart, bucinnazine, dextrose and sodium chloride injection, domperidone, entecavir, fentanyl, furosemide, glutathione, glycyrrhizic acid, granisetron, lappaconitine, levoglutamide, metoclopramide, mosapride, omeprazole, oxycocet, oxycodone, pantoprazole, paraffin liquid, polyene phosphatidylcholine, potassium, promethazine, sodium chloride, unspecified herbal and traditional medicine (simo decoction), and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed mass at right shoulder girdle, multiple liver lesions, and retroperitoneal and pancreas lymphadenopathies. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 03 Dec 2014 (Day –2), the subject experienced upper abdominal pain (Grade 1). On 05 Dec 2014 (Day 1), the subject experienced nausea (Grade 1), decreased appetite (Grade 1), and the severity of upper abdominal pain worsened to Grade 2. On the same day (Day 1), the severity of upper abdominal pain improved to Grade 1 and the subject also recovered from nausea. The subject was treated with oxycodone, metoclopramide, lappaconitine, bucinnazine, bacillus lichenformis, unspecified herbal and traditional medicine (simo decoction), potassium, and mosapride. On 08 Dec 2014 (Day 4), the subject experienced fatigue (Grade 1). On 10 Dec 2014 (Day 6), the subject experienced nausea (Grade 1) and vomiting (Grade 1). The subject was treated with metoclopramide, aluminum phosphate, granisetron, levoglutamide, pantoprazole, and domperidone. The study drug dose was not changed. On 31 Dec 2014 (Day 27), severity of upper abdominal pain worsened to Grade 2 and the subject also experienced increased aspartate aminotransferase (Grade 2), increased alanine aminotransferase (Grade 1), increased blood bilirubin (Grade 3), increased blood alkaline phosphatase (Grade 2), increased gamma-glutamyltransferase (Grade 3), increased lactate dehydrogenase (Grade 1), and electrocardiogram QT prolonged (Grade 1). Laboratory results showed ALP 339 U/L (NR: 43 – 115), ALT 73 U/L (NR: 10 – 40), AST 204 U/L (NR: 10 – 43), total bilirubin 73.4 umol/L (NR: 1.7 – 18.8), CRP 32.9 mg/L (NR: 0 – 5), GGT 502 U/L (NR: 10 – 49), and alpha fetoprotein > 72604.1 ug/L (NR: 0 – 6.1). The subject was treated with glutathione, ursodeoxycholic acid, and glycyrrhizic acid. On the same day (Day 27), tumor response assessment showed disease progression. On 01 Jan 2015 (Day 28), the subject was withdrawn from study due to disease progression and received last dose of the study drug on the same day (Day 28). On 01 Jan 2015 (Day 28), the severity of upper abdominal pain

worsened to Grade 3, increased blood alkaline phosphatase improved to Grade 1, and increased blood bilirubin improved to Grade 2, and the subject also experienced constipation (Grade 2). On the same day (Day 28), the subject recovered from increased lactate dehydrogenase and increased alanine aminotransferase. The subject was treated with liquid paraffin, bucinnazine, glycyrrhizic acid, and promethazine. On 02 Jan 2015 (Day 29), the subject experienced insomnia (Grade 1) and severity of upper abdominal pain improved to Grade 2 and received sodium chloride, fentanyl, and promethazine. On 06 Jan 2015 (Day 33), severity of increased aspartate aminotransferase and increased blood bilirubin worsened to Grade 3; and increased blood alkaline phosphatase worsened to Grade 2. The subject was treated with ursodeoxycholic acid. The subject did not recover from nausea, vomiting, upper abdominal pain, decreased appetite, fatigue, increased aspartate aminotransferase, increased gamma-glutamyltransferase, increased blood alkaline phosphatase, constipation, insomnia, electrocardiogram QT prolonged, and increased blood bilirubin. The Investigator considered decreased appetite nonserious and possibly related to the study drug; nausea, vomiting, and fatigue nonserious and probably related to the study drug; upper abdominal pain, increased aspartate aminotransferase, increased gamma-glutamyltransferase, increased blood alkaline phosphatase, insomnia, increased lactate dehydrogenase, increased alanine aminotransferase, and increased blood bilirubin nonserious and not related to the study drug but related to disease progression; constipation, electrocardiogram QT prolonged nonserious and not related to the study drug.

On 28 Jan 2015 (Day 55, 27 days after the last dose), the subject died due to malignant neoplasm progression (metastatic HCC unknown). Autopsy was not performed. The Investigator considered this event serious and not related to the study drug but related to disease progression.

Subject Number	24161016
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-019505
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 62-year-old Chinese female was diagnosed with hepatocellular carcinoma on 29 Oct 2014. Significant medical history included chronic hepatitis B and epigastric discomfort. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included ambroxol, aminomethylbenzoic acid, articure, ascorbic acid, bismuth, bromhexine, cough and cold preparations (compound codeine platycodon), dezocine, digestives incl. enzymes (compound digestive enzymes), enemas, entecavir, etamsilate, fentanyl, fluconazole, glutathione, glycyrrhizic acid, human albumin, lactulose, methoxyphenamine, morphine, omeprazole, ondansetron, phytomenadione, potassium, potassium citrate, proliv, pyridoxine, sophora spp., tiopronin, torasemide, tramadol, unspecified herbal and traditional medicine (xinhuang tabella), and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe and masses in bilateral lower lobes of lung. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 20 Nov 2014 (Day 15), the subject experienced increased aspartate aminotransferase (Grade 2) with AST 171 U/L (NR: 10 – 36) and increased blood bilirubin (Grade 1) with total bilirubin 24.5 umol/L (NR: 1.7 – 18.8). On 02 Dec 2014 (Day 27), increased blood bilirubin worsened to Grade 2 with total bilirubin 48.4 umol/L and the subject also experienced increased international normalized ratio (Grade 1) with INR 1.3 (NR: 0.9 – 1.1). On 16 Dec 2014 (Day 41), tumor response assessment showed disease progression. On same day (Day 41), the severity of increased aspartate aminotransferase increased to Grade 3. On 17 Dec 2014 (Day 42), the subject experienced lung infection (Grade 1). The subject was treated with glutathione, omeprazole, ambroxol, cough and cold preparations, methoxyphenamine, bromhexine, etamsilate, aminomethylbenzoic acid, and phytomenadione. The subject did not recover from increased aspartate aminotransferase, increased blood bilirubin, and increased international normalized ratio. On 22 Dec 2014 (Day 47), the subject received the last dose due to disease progression. On 27 Dec 2014 (Day 52), the subject recovered from lung infection. The Investigator considered increased aspartate aminotransferase, increased blood bilirubin nonserious and possibly related to the study drug; increased international normalized ratio nonserious and probably related to the study drug; lung infection nonserious and not related to the study drug.

On 29 Dec 2014 (Day 54, 7 days after the last dose), the subject died due to malignant neoplasm progression. The Investigator considered malignant neoplasm progression serious and not related to the study drug but related to disease progression.

Subject Number	24221002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-019365
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 67-year-old Chinese male was diagnosed with hepatocellular carcinoma on 26 Jun 2014. Significant medical history included abdominal distension, increased alanine aminotransferase, increased blood alkaline phosphatase, increased aspartate aminotransferase, increased gamma-glutamyltransferase, decreased hemoglobin, decreased red blood cell count, and hepatitis B. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included amino acids (compound amino acid injection), domperidone, fats (fat emulsion injection), and vitamin B-complex with vitamin C. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes; lymphadenopathy at right branch of portal vein. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 11 Aug 2014 (Day –3), the subject had increased gamma-glutamyltransferase (Grade 1). Laboratory tests showed ALP 156 U/L (NR: 43 – 115) and GGT 118 U/L (NR: 10 – 49). The subject did not recover from the event. The Investigator considered the event nonserious and not related to study drug.

On 14 Aug 2014 (Day 1), treatment with study drug was initiated.

On 26 Aug 2014 (Day 13), the subject experienced decreased appetite (Grade 1). On 28 Aug 2014 (Day 15), the subject experienced vomiting (Grade 2) and decreased blood albumin (Grade 1). Laboratory tests showed albumin 30 g/L (NR: 35 – 55), chloride 85 mmol/L (NR: 95 – 110), and sodium 123 mmol/L (NR: 133 – 145). The subject was treated with intravenous amino acids, fat emulsion injection, and vitamin B-complex with vitamin C. The study drug dose did not change. The subject did not recover from these events. The Investigator considered vomiting and decreased appetite nonserious and possibly related to study drug; decreased blood albumin nonserious and probably related to the study drug.

On 11 Sep 2014 (Day 29), the study drug was interrupted due to clinical disease progression. On 12 Sep 2014 (Day 30), the subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of study drug on 10 Sep 2014 (Day 28).

On 28 Sep 2014 (Day 46, 18 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. The Investigator considered this event serious and not related to the study drug but related to disease progression.

Subject Number	24231003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-018599
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 41-year-old Chinese male was diagnosed with hepatocellular carcinoma on 10 Nov 2014. Significant medical history included hepatitis B and varicose veins (left lower extremity varicose veins). Previous anticancer therapy included hepatectomy. Prior and concomitant medications included alanyl glutamine, brucea javanica, diisopropylamine, lansoprazole, oxycocet, propofol, thymalfasin, unspecified herbal and traditional medicine (bozhi glycopeptide), and vitamins. 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 20 Dec 2014 (Day 1), treatment with study drug was initiated.

On 15 Jan 2015 (Day 27), the subject experienced hypoalbuminemia (Grade 1) with albumin 34 g/L (NR: 35 – 55). On 30 Jan 2015 (Day 42), the subject experienced flank pain (Grade 2) and was treated with oxycocet. On 02 Feb 2015 (Day 45), the subject experienced increased aspartate aminotransferase (Grade 1), increased blood bilirubin (Grade 2), and proteinuria (Grade 1). Laboratory tests showed albumin 33 g/L, ALP 245 U/L (NR: 43 – 115), ALT 31 U/L (NR: 10 – 40), AST 61 U/L (NR: 10 – 43), total bilirubin 40.7 umol/L (NR: 0 – 18.8), total protein 82 g/L (NR: 60 – 80), and GGT 345 U/L (NR: 10 – 49). The study drug dose did not change. On the same day (Day 45), tumor response assessment showed disease progression. On 03 Feb 2015 (Day 46), the subject experienced hepatorenal syndrome (Grade 3). Laboratory tests showed 24h urine protein 0.4131 g/24hr. On the same day (Day 46), the subject was withdrawn from study drug due to disease progression and received the last dose of the study drug. The subject did not recover from these events. The Investigator considered hepatorenal syndrome, flank pain, and hypoalbuminemia nonserious and not related to the study drug, but related to disease progression; increased aspartate aminotransferase, increased blood bilirubin, and proteinuria nonserious and not related to the study drug.

On 03 Mar 2015 (Day 74, 28 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. The Investigator considered this event serious and not related to the study drug but related to disease progression.

Subject Number	24231008
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003298
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Multiple organ dysfunction syndrome
Non-Fatal SAE(s)	Hypoproteinaemia, Multiple organ dysfunction syndrome
AE(s) Leading to Discontinuation	Multiple organ dysfunction syndrome
Death due to PD	Yes

A 51-year-old Chinese male was diagnosed with hepatocellular carcinoma on 23 Sep 2014. Significant medical history included cough, hepatitis B, and right upper abdominal pain. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included alanyl glutamine, ambroxol, amino acids w/fats/glucose, aminophylline, antihemorrhagics, bicart, chymotrypsin, codeine, combicin, cough and cold preparations, deslanoside, dexamethasone, fats, fructose, furosemide, glucose injection, glyceryl trinitrate, human albumin, hydrochlorothiazide, insulin, lidocaine, metoclopramide, morphine, octreotide, potassium aspartate, proliv, sodium chloride, spironolactone, torasemide, ubenimex, and unspecified herbal and traditional medicine (fufangbanmaojiaonang). At Screening, tumor assessments of target/non-target lesions via CT scan showed lung nodule metastasis and retroperitoneal lymphadenopathy. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

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

On 07 Jan 2015 (Day 8), the subject experienced peripheral edema (Grade 1). The subject was treated with hydrochlorothiazide and spironolactone. On 11 Jan 2015 (Day 12), the subject experienced hypoproteinemia (Grade 2) and asthenia (Grade 1). The subject was treated with furosemide and human albumin. On 12 Jan 2015 (Day 13), laboratory tests showed total protein 65.96 g/L (NR: 60 – 88), creatinine 133 umol/L (NR: 53 – 115), and total bilirubin 30.8 umol/L (NR: 0 – 20.5). The study drug dose did not change. The subject did not recover from peripheral edema and hypoproteinemia. On 17 Jan 2015 (Day 18), the subject recovered from asthenia. The Investigator considered hypoproteinemia serious (life threatening) and not related to the study drug; peripheral edema and asthenia nonserious and not related to the study drug.

On 20 Jan 2015 (Day 21), the subject was hospitalized for multiple organ dysfunction syndrome (Grade 4) and also experienced lung infection (Grade 3) with symptoms of dyspnea. The CT scan of chest showed bilateral pleural effusion and acute pulmonary edema. The subject underwent pleural effusion puncture drainage and also was treated with combicin, deslanoside, glyceryl trinitrate, torasemide, and aminophylline. On 21 Jan 2015 (Day 22), the subject's dyspnea aggravated and the subject was treated with high flow oxygen therapy. The aggravated dyspnea alleviated after symptomatic treatment. Chest x-ray showed bilateral pneumothorax and the subject underwent bilateral pleural effusion drainage. On the same day (Day 22), laboratory tests were done and showed albumin 31.1 g/L (NR: 37 – 53), ALT 73.07 U/L (NR: 0 – 40),

AST 113.6 U/L (NR: 0 – 40), total bilirubin 80.97 umol/L, creatinine 215.5 umol/L, LDH 450 U/L (NR: 119 – 229), and total protein 54.3 g/L. On 21 Jan 2015, (Day 22), the subject died due to multiple organ dysfunction syndrome secondary to clinical disease progression and received the last dose of the study drug on the same day (Day 22). Autopsy was not performed. At the time of death, the subject had not recovered from lung infection. The Investigator considered multiple organ dysfunction syndrome serious and not related to the study drug but related to disease progression; lung infection nonserious and not related to the study drug.

Subject Number	24231009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-018604
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 70-year-old Chinese male was diagnosed with hepatocellular carcinoma on 08 Nov 2014. Significant medical history included ascites, bronchitis, duodenal ulcer, hepatitis C, hepatic cyst, hepatic cirrhosis, decreased total protein, prostatitis, rib fracture, upper abdominal pain (right), and vertigo. Previous anticancer therapies included cinobufacini injection and transcatheter arterial chemoembolization. Prior and concomitant medications included ademetionine, glutathione, glycyrrhizic acid, human albumin, lansoprazole, octreotide, oxycocet, and unspecified herbal and traditional medicine (huganning capsule, hui-sheng oral liquid, and xiyanping injection). At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left liver lobe. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 08 Jan 2015 (Day 1), treatment with study drug was initiated.

On 06 Feb 2015 (Day 30), the subject experienced asthenia (Grade 1), decreased lymphocyte count (Grade 3), and decreased platelet count (Grade 1). On the same day (Day 30), laboratory tests showed platelet count 82 x10^9/L (NR: 125 – 375) and absolute lymphocytes count 0.3 x10^9/L (NR: 0.9 – 3.6). The study drug dose did not change. The subject did not recover from asthenia, decreased lymphocyte count and was recovering from decreased platelet count. The Investigator considered decreased lymphocyte count and decreased platelet count nonserious and probably related to the study drug; asthenia nonserious and not related to the study drug.

On 04 Mar 2015 (Day 56), the subject experienced abdominal pain (Grade 3) and abdominal distension (Grade 2). The subject was treated with oxycocet. The study drug dose did not change. The subject did not recover from these events. The Investigator considered these events nonserious and not related to the study drug but related to disease progression.

On 05 Mar 2015 (Day 57), the subject was withdrawn from study due to clinical disease progression and received the last dose of the study drug on the same day (Day 57).

On 07 Mar 2015 (Day 59, 2 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. The Investigator considered malignant neoplasm progression serious and not related to the study drug but related to disease progression.

Subject Number	30061008
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001653
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Non-Fatal SAE(s)	Back pain
Death due to PD	Yes

A 52-year-old Asian male was diagnosed with hepatocellular carcinoma on 16 Apr 2013. Significant medical history included abdominal pain, decreased appetite, chronic gastritis, chronic hepatitis B, constipation, hypertension, hepatic cirrhosis, low back pain, and gastroesophageal reflux disease. Previous anticancer therapies included transcatheter arterial chemoembolization, tumor excision, radiotherapy to right liver lobe and retroperitoneal lymph nodes. Prior and concomitant medications included acetylcysteine, amino acids, amlodipine, benzydamine, calcitonin, camostat, carmellose, cefotaxime, chlorhexidine, chlorphenamine, chlorpromazine, cimetropium, de shuang, dexamethasone, diosmectite, dynamag, fentanyl, festal plus, flumazenil, furosemide, glucose, hepatamine, human albumin, itopride, lactobacillus acidophilus, lactulose, lidocaine, lorazepam, magnesium oxide, megestrol, metoclopramide, metronidazole, midazolam, montmorillonite, morphine, nystatin, oxycodone, pamidronic acid, pancreatin, pantoprazole, paracetamol, pethidine, phytomenadione, potassium, pronase, propacetamol, ranitidine, rifaximin, simeticone, smoflipid, spironolactone, tamsulosin, telbivudine, thiamine, ursodeoxycholic acid, and vitamins. At Screening, tumor assessments of target/non-target lesions via CT scan showed mass at right middle lung lobe and lymphadenopathy at right hilar; MRI scan showed lesions at right and left lobe of liver, lumbar vertebral mass, para-aortic, para-caval, retroperitoneal, and diaphragmatic lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 10 Oct 2014 (Day 1), treatment with study drug was initiated.

On 20 Oct 2014 (Day 11), the subject was hospitalized for aggravation of low back pain (Grade 3) and was treated with fentanyl and pethidine. On the same day (Day 11), the subject underwent palliative radiotherapy to the spine (T12 – L5) for the low back pain. On 22 Oct 2014 (Day 13), the subject experienced limb edema (Grade 2). On 24 Oct 2014 (Day 15), the subject experienced hyponatremia (Grade 3) with sodium 128 mmol/L (NR: 133 – 145). The subject was treated with furosemide, spironolactone, human albumin, and metoclopramide. On 26 Oct 2014 (Day 17), the subject experienced nausea (Grade 3). On the same day (Day 17), the study drug was interrupted due to nausea. On 05 Nov 2014 (Day 27), nausea improved to Grade 2. On 06 Nov 2014 (Day 28), the study drug was resumed at same dose. The subject did not recover from aggravation low back pain, limb edema, hyponatremia, and nausea. The Investigator considered aggravation of low back pain serious and not related to the study drug, but related to disease progression with metastasis to T5 – T12; hyponatremia nonserious and not related to the study drug; nausea, nonserious and probably related to the study drug; limb edema nonserious and possibly related to the study drug.

On 19 Nov 2014 (Day 41), the subject experienced increased aspartate aminotransferase (Grade 2) with AST 170 U/L (NR: 10 – 43) and increased blood bilirubin (Grade 2) with total bilirubin 27.2 umol/L (NR: 1.7 – 18.8). On 21 Nov 2014 (Day 43), the subject experienced right shoulder pain (Grade 2). On 26 Nov 2014 (Day 48), the study drug was interrupted due to increased blood bilirubin. On 03 Dec 2014 (Day 55), tumor response assessment showed disease progression. On 07 Dec 2014 (Day 59), the subject experienced hypercalcemia (Grade 3), hyponatremia (Grade 1), and decreased platelet count (Grade 3). Laboratory tests showed calcium 2.98 mmol/L (NR: 2.12 – 2.62), AST 136 U/L, and albumin 31 g/L (NR: 35 – 55). On 08 Dec 2014 (Day 60), the subject was given platelet transfusion. On 08 Dec 2014 (Day 60), the subject was withdrawn from the study due to disease progression. The subject received the last dose of the study drug on 25 Nov 2014 (Day 47). On 09 Dec 2014 (Day 61), the subject experienced hepatic encephalopathy (Grade 3) and hypercalcemia improved to Grade 2. The subject was treated with de shuang, amino acids (aspargine-L-ornithine), calcitonin, dexamethasone, lactulose, and pamidronic acid. On 10 Dec 2014 (Day 62), increased aspartate aminotransferase worsened to Grade 3 with AST 212 U/L (NR: 10 – 40). On the same day (Day 62), the subject was given platelet transfusion. On 12 Dec 2014 (Day 64), increased blood bilirubin worsened to Grade 3 with total bilirubin 80.541 umol/L (NR: 1.71 – 20.52). On 15 Dec 2014 (Day 67), the subject experienced prolonged activated partial thromboplastin time (Grade 1) and was given platelet transfusion. The subject did not recover from increased aspartate aminotransferase, increased blood bilirubin, right shoulder pain, hypercalcemia, decreased platelet count, hepatic encephalopathy, and prolonged activated partial thromboplastin time. The Investigator considered increased aspartate aminotransferase, increased blood bilirubin, right shoulder pain, hypercalcemia, hyponatremia, decreased platelet count, hepatic encephalopathy, and prolonged activated partial thromboplastin time nonserious and not related to the study drug.

On 19 Dec 2014 (Day 71, 24 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. The Investigator considered this event serious and not related to the study drug.

Subject Number	30071003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-016991
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Death due to PD	Yes

A 43-year-old Asian male was diagnosed with hepatocellular carcinoma on 07 Sep 2013. Significant medical history included chronic hepatitis C, erosive gastritis, hypertension, liver biopsy, hepatic cirrhosis, and hepatitis B. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included amlodipine, calcium gluconate, carvedilol, chlorhexidine, fentanyl, furosemide, hepatamine, human albumin, human insulin, hydrocortisone, hydromorphone, loperamide, megestrol, metoclopramide, morphine, pangest f, rabeprazole, silybum marianum, spironolactone, tenofovir, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, right portal vein, and right hepatic vein; right adrenal mass; right anterior cardio hepatic, porta-hepatis, and portocaval lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 12 Nov 2013 (Day 1), treatment with study drug was initiated.

On 06 Feb 2014 (Day 87), the subject experienced hypertension (Grade 2) with BP of 146/89 mmHg and was treated with carvedilol and amlodipine. On 13 Feb 2014 (Day 94), the subject experienced ascites (Grade 2) and was treated with furosemide, human albumin, and spironolactone. Laboratory tests showed albumin 35 g/L (NR: 35 – 55), ALP 223 U/L (NR: 43 – 115), and AST 138 U/L (NR: 10 – 43). On 06 Mar 2014 (Day 115), the study drug was reduced to 600 mg/day due to ascites. The subject underwent paracentesis. On 19 Mar 2014 (Day 128), ascites worsened to Grade 3 and the subject also experienced decreased appetite (Grade 2). On 03 Apr 2014 (Day 143), the study drug dose was reduced to 400 mg/day due to ascites and decreased appetite. On the same day (Day 143), the subject experienced decreased weight (Grade 1) with body weight of 60.2 kg (Baseline: 64 kg). On the same day (Day 143), the subject recovered from hypertension. On 16 Apr 2014 (Day 156), the subject underwent repeat paracentesis and ascites improved to Grade 2. On 21 Apr 2014 (Day 161), the subject experienced diarrhea (Grade 1) and was treated with loperamide. On 30 Apr 2014 (Day 170), subject's decreased weight worsened to Grade 2 with body weight of 55 kg. The subject was treated with metoclopramide, megestrol, and rabeprazole. On 20 May 2014 (Day 190), the subject experienced fatigue (Grade 3). On 24 May 2014 (Day 194), the study drug was interrupted due to fatigue and decreased appetite. On 26 May 2014 (Day 196), the severity of decreased appetite and decreased weight worsened to Grade 3 with body weight of 48 kg. On 09 Jun 2014 (Day 210), the subject experienced hyperkalemia (Grade 2) with potassium 5.9 mmol/L (NR: 3.5 – 5.5) and hypotension (Grade 2) with BP 77/55 mmHg. The subject was treated with calcium gluconate, human insulin, and hepatamine. The subject did not recover from ascites, decreased appetite, decreased weight, diarrhea, fatigue, hyperkalemia, and hypotension. The Investigator considered

hypertension, ascites, decreased appetite, and diarrhea nonserious and possibly related to the study drug; fatigue nonserious and possibly related to the study drug and related to disease progression; hyperkalemia and hypotension nonserious and not related to the study drug but related to disease progression; decreased weight nonserious and not related to the study drug.

On 10 Jun 2014 (Day 211), the subject was withdrawn from study due to clinical disease progression. The subject received the last dose of the study drug on 23 May 2014 (Day 193).

On 13 Jun 2014 (Day 214, 21 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. The Investigator considered malignant neoplasm progression serious and not related to the study drug but related to disease progression.

Subject Number	30121002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01493-CLI-KR
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Non-Fatal SAE(s)	Jaundice
AE(s) Leading to Discontinuation	Jaundice
Death due to PD	Yes

A 65-year-old Asian female was diagnosed with hepatocellular carcinoma on 07 Oct 2013. Significant medical history included hepatitis B, hepatic cirrhosis, and splenomegaly. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included aceclofenac, aciclovir, amino acids, cefotaxime, chlorphenamine, desonide, ecabet, falkamin, fentanyl, furosemide, hydroxyzine, metronidazole, minerals w/vitamins, morphine, pantoprazole, pennel, pethidine, silybum marianum, spironolactone, targin, tenofovir, terlipressin, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed peritoneum lymphadenopathy and lesion at quadrate lobe of liver. The BCLC stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 23 Oct 2013 (Day 1), treatment with study drug was initiated.

On 07 May 2014 (Day 197), the subject was hospitalized for jaundice (Grade 2). Laboratory tests showed ALT 129 U/L (NR: 10 – 33), AST 360 U/L (NR: 10 – 36), ALP 349 U/L (NR: 30 – 115), GGT 297 U/L (NR: 5 – 32), urobilinogen 1 mg/dL, urine bilirubin dipstick 3+, and total bilirubin 300.96 umol/L (NR: 0.171 – 18.81). The study drug was interrupted due to jaundice. Treatment included falkamin, pennel, and silybum marianum. On 11 May 2014 (Day 201), serum bilirubin was 16.97 mg/dL (NR: Not provided). On the same day (Day 201), the subject was withdrawn from study due to clinical disease progression and received the last dose of study drug on 06 May 2014 (Day 196). On 11 May 2014 (Day 201, 5 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. At the time of death the subject had not recovered from jaundice. The Investigator considered malignant neoplasm and jaundice serious and not related to study drug but related to disease progression.

Subject Number	30161007
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01506-CLI-KR
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Malignant neoplasm progression
Non-Fatal SAE(s)	Neck pain
Death due to PD	Yes

A 70-year-old Asian female was diagnosed with hepatocellular carcinoma on 04 Mar 2014. Significant medical history included diabetes mellitus, hepatitis B, hypertension, hepatic cirrhosis, and posterior neck pain. Previous anticancer therapy included radiotherapy to cervical vertebral lesion (3 – 5). Prior and concomitant medications included afloqualone, amlodipine, camostat, cimetropium, diapride forte, glimepiride, lidocaine, megestrol, oxycodone, rebamipide, silybum marianum, simeticone, ultracet, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right and left liver lobes, cervical metastases, and lung mass at aorto-pulmonary window. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 19 May 2014 (Day 22), the subject was hospitalized for neck pain (Grade 3). On 21 May 2014 (Day 24), tumor response assessment showed disease progression. On 22 May 2014 (Day 25), the subject was withdrawn from the study due to disease progression and the subject received the last dose of the study drug on the same day. The subject received palliative radiotherapy to cervical spine (c-spine 4). The subject did not recover from neck pain. The Investigator considered neck pain serious and not related to the study drug but related to disease progression.

On 09 Jun 2014 (Day 43, 18 days after the last dose), the subject died due to malignant neoplasm progression. Autopsy was not performed. The Investigator considered this event serious and not related to the study drug but related to disease progression.

Subject Number	32041002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003482
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Liver carcinoma ruptured
Non-Fatal SAE(s)	Liver carcinoma ruptured
Death due to PD	Yes

A 37-year-old Asian male was diagnosed with hepatocellular carcinoma on 31 Mar 2014. Significant medical history included diabetes mellitus, hepatitis B, hepatic cirrhosis, insomnia, and pulmonary embolism. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included ceftriaxone, duovent, enoxaparin, furosemide, glipizide, human mixtard, lactulose, lamivudine, lorazepam, magnesium hydroxide, metformin, metronidazole, midazolam, morphine, norgesic, paracetamol, pioglitazone, and senna alexandrina. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of the liver. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 10 Jul 2014 (Day 1), treatment with study drug was initiated.

On 05 Oct 2014 (Day 88), the subject experienced left upper quadrant tumor pain (Grade 1) and was treated with norgesic. The study drug dose was not changed. The subject did not recover from this event. The Investigator considered this event nonserious and not related to the study drug.

On 27 Oct 2014 (Day 110), tumor response assessment showed disease progression. On 30 Oct 2014 (Day 113), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 29 Oct 2014 (Day 112).

On 11 Nov 2014 (Day 125), the subject was hospitalized for ruptured liver carcinoma (suspected rupture hepatoma; Grade 3). Laboratory tests showed ALT 24 U/L (NR: 0 – 41), AST 126 U/L (NR: 0 – 40), ALP 192 U/L (NR: 40 – 129), total bilirubin 15.561 umol/L (NR: 0 – 17.1), and Hct 0.22 L/L (NR: 0.36 – 0.5). The subject was treated with packed red blood cell transfusion, fresh frozen plasma transfusion, oxygen therapy, morphine, ceftriaxone, metronidazole, paracetamol, duovent, and midazolam. On 25 Nov 2014 (Day 139, 27 days after the last dose), the subject died due to ruptured liver carcinoma secondary to disease progression. Autopsy was not performed. The Investigator considered ruptured liver carcinoma serious and not related to the study drug.

Subject Number	44031006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001323
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Hepatic failure
Non-Fatal SAE(s)	Hepatic failure
Death due to PD	Yes

A 42-year-old Asian male was diagnosed with hepatocellular carcinoma on 20 Nov 2013. Significant medical history included hepatitis B. Previous anticancer therapy included radiotherapy treatment. Prior and concomitant medications included augmentin, benzydamine, loperamide, midazolam, naproxen, omeprazole, paracetamol, phospholipids, tenofovir, and urea. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of the liver and bilateral lower lobes of the lung. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 17 Apr 2014 (Day 1), treatment with study drug was initiated.

On 01 Oct 2014 (Day 168), tumor response assessment showed disease progression. On 02 Oct 2014 (Day 169), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on 01 Oct 2014 (Day 168).

On 26 Oct 2014 (Day 193), the subject experienced dyspnea (Grade 3), abdominal distension (Grade 3) and was hospitalized with a diagnosis of hepatic failure (Grade 3). The subject's liver function tests were worsening and treatment was given but source document for liver function tests and treatment cannot be obtained. On 28 Oct 2014 (Day 195), the subject recovered from dyspnea. On 30 Oct 2014 (Day 197, 29 days after the last dose), the subject died due to hepatic failure secondary to disease progression. Autopsy was not performed. At the time of death, the subject had not recovered from abdominal distention. The Investigator considered hepatic failure serious and not related to the study drug; dyspnea and abdominal distention nonserious and not related to the study drug.

Subject Number	45011004
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01463-CLI-TW
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Sudden death
AE(s) Leading to Discontinuation	Sudden death
Death due to PD	No

A 62-year-old Chinese male was diagnosed with hepatocellular carcinoma on 05 Mar 2013. Significant medical history included chronic hepatitis B, constipation, gastritis, and hepatic cirrhosis. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included aluzaine, dextromethorphan, entecavir, esomeprazole, levocetirizine, metoclopramide, neotracin, nifedipine, pantoprazole, paracetamol, sennoside a+b, silybum marianum, simeticone, strocain, ultracet, and urea. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

On 11 Dec 2013 (Day 1), treatment with study drug was initiated.

On 24 Dec 2013 (Day 14), subject experienced hypertension (Grade 3) with blood pressure of 162/92 mmHg and was treated with nifedipine. On 02 Jan 2014 (Day 23), the study drug dose was missed by the subject. On the same day (Day 23), the severity of hypertension improved to Grade 2. On 03 Jan 2014 (Day 24), the study drug was resumed at the same dose. The subject did not recover from this event. The Investigator considered this event nonserious and possibly related to the study drug.

On 04 Feb 2014 (Day 56), the QTcF was 447 msec and at Screening, QTcF was 427 msec. On 27 Feb 2014 (Day 79), the subject experienced a fall (Grade 2) in the bathroom for an unknown cause. A few hours later, the subject was brought to the emergency room for further evaluation however the subject had no blood pressure, heart rate or respiratory rate. The subject had a sudden death (unknown cause) and the secondary cause of death was hepatocellular carcinoma. The subject received the last dose of the study drug on the same day (Day 79). Autopsy was not performed. The Investigator considered sudden death serious and possibly related to the study drug; fall nonserious and possibly related to study drug.

Subject Number	45081001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01446-CLI-TW
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Respiratory failure
Non-Fatal SAE(s)	Infectious pleural effusion, Pleural effusion, Abdominal distension
Death due to PD	Yes

An 82-year-old Chinese male was diagnosed with hepatocellular carcinoma on 30 Oct 2008. Significant medical history included acquired spondylolisthesis, anxiety, benign prostatic hyperplasia, diabetes mellitus, esophagitis, hepatic steatosis, gallbladder polyp, chronic hepatitis B, left and right renal cyst, lumbosacral spondylosis without myelopathy, melanosis coli, hemorrhoids, myalgia, myositis, cerebrovascular accident, peptic ulcer, uncomplicated senile dementia, and urethral stenosis. Previous anticancer therapies included hepatectomy, percutaneous ethanol injection therapy, transcatheter arterial chemoembolization, and radiotherapy to right lobe of liver. Prior and concomitant medications included acetylcysteine bethanechol, ceftazidime, cefuroxime, clonazepam, fentanyl, flunarizine, furosemide, human albumin, pramipexole, quetiapine, ristfor, sodium chloride, strocain, tamsulosin, and ultracet. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right lobes of liver and masses at right lower lobe of lung and pancreas. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 20 Dec 2013 (Day 1), treatment with study drug was initiated.

On 21 Jan 2014 (Day 33), the subject experienced bullous dermatitis (Grade 1) and the study drug was reduced to 400 mg/day due to this event. Treatment was not provided. On 28 Jan 2014 (Day 40), the subject recovered from this event. The Investigator considered bullous dermatitis nonserious and probably related to study drug.

On 29 Jan 2014 (Day 41), the subject experienced pleuritic pain (Grade 2). On 31 Jan 2014 (Day 43), the subject was hospitalized for infectious pleural effusion (left thoracic empyema; Grade 3) and pleural effusion (left; Grade 3) and the study drug was interrupted due to these events. Chest x-ray and chest CT scan showed marked left pleural effusion. The subject underwent pleural decortication and tube thoracostomy. Treatment included ultracet, strocain, cefuroxime, acetylcysteine, and sodium chloride. On 02 Feb 2014 (Day 45), the study drug was resumed at the same dose. On 04 Feb 2014 (Day 47), the subject recovered from pleuritic pain and was discharged from the hospital. On 21 Feb 2014 (Day 64), the subject underwent left thoracic cavity drainage. On 23 Feb 2014 (Day 66), the severity of pleural effusion improved to Grade 2. The subject did not recover from infectious pleural effusion and pleural effusion. The Investigator considered pleural effusion and infectious pleural effusion serious and not related to study drug; pleuritic pain nonserious and not related to study drug.

On 21 Feb 2014 (Day 64), the subject stopped taking the study drug for unknown reason. The subject received the last dose of study drug on 20 Feb 2014 (Day 63). On 24 Feb 2014 (Day 67), the subject withdrew from the study by choice.

On 25 Feb 2014 (Day 68), the subject was hospitalized for abdominal distension (Grade 2) and also experienced peripheral edema (edema limbs; Grade 2) and sepsis (Grade 4). Chest x-ray showed progression of pleural effusion and bilateral increased infiltration. Treatment included fentanyl and furosemide. On 28 Feb 2014 (Day 71), the subject recovered from sepsis. On 01 Mar 2014 (Day 72), the subject was discharged from the hospital. The subject did not recover from peripheral edema and abdominal distension. The Investigator considered abdominal distension serious and not related to the study drug; peripheral edema and sepsis nonserious and not related to the study drug.

On 10 Mar 2014 (Day 81), the subject experienced respiratory failure and was admitted to hospice. Later that day, (Day 81, 18 days after the last dose), the subject died due to respiratory failure. It was unknown if autopsy was performed. The Investigator considered respiratory failure serious and not related to study drug but related to disease progression.

Subject Number	45121006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000765
Assigned Treatment	Sorafenib 800 mg/day
Fatal SAE(s)	Acute respiratory failure
Non-Fatal SAE(s)	Sepsis, Abdominal pain, Decreased appetite, Ascites
AE(s) Leading to Discontinuation	Abdominal pain, Ascites
Death due to PD	Yes

A 62-year-old Chinese male was diagnosed with hepatocellular carcinoma on 05 Jun 2012. Significant medical history included duodenal ulcer, gastroesophageal reflux disease, hepatitis B, and hypertension. Previous anticancer therapies included radiofrequency ablation and transcatheter arterial chemoembolization. Prior and concomitant medications included alprazolam, amlodipine, ascorbic acid, brown mixture, ceftibuten, dextrose and sodium chloride injection, dextrose w/dopamine, diphenhydramine, dopamine, entecavir, epinephrine, famotidine, fentanyl, flomoxef, furosemide, glucose, human albumin, intravenous solution additives, ipratropium, lansoprazole, loperamide, lorazepam, megestrol, metoclopramide, metronidazole, morphine, moxifloxacin, nystatin, paracetamol, pethidine, potassium, propranolol, simeticone, sodium chloride, spironolactone, tamsulosin, terbutaline, tramadol, tranexamic acid, ultracet, and unacid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at segments 2 – 3, 2 – 4, and 5 of the liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

On 15 Aug 2014 (Day 1), treatment with study drug was initiated.

On 02 Oct 2014 (Day 49), the subject was hospitalized for sepsis (Grade 4) associated with fever and dyspnea. The study drug was interrupted due to this event. Laboratory result showed WBC 14.26 x10^9/L (NR: 4.5 – 11) and blood culture was positive for salmonella group B and gram-negative bacilli. Chest x-ray showed prominence of bilateral hilar shadows. The subject was treated with paracetamol, metronidazole, flomoxef, lansoprazole, and ultracet. On 06 Oct 2014 (Day 53), the study drug was resumed at the same dose. On 09 Oct 2014 (Day 56), the subject recovered from this event. The Investigator considered sepsis serious and not related to study drug. The Investigator clarified that the source of sepsis was unknown.

On 29 Aug 2014 (Day 15), the subject experienced abdominal pain (Grade 1) and on 15 Oct 2014 (Day 62), the subject was hospitalized for increased severity of abdominal pain (Grade 3). On 16 Oct 2014 (Day 63), study drug was reduced to 400 mg/day due to this event. Blood culture was negative. The subject was treated with amlodipine, entecavir, ultracet, flomoxef, lansoprazole, tramadol, dextrose, and sodium chloride injection. On 19 Oct 2014 (Day 66), the study drug dose was increased back to 800 mg/day as instructed by the Investigator. On 21 Oct 2014 (Day 68), the abdominal pain improved to Grade 2 and the subject was discharged from the hospital. The Investigator considered abdominal pain serious and not related to study drug.