superficial thrombophlebitis serious and not related to study drug; pain in extremity nonserious and not related to study drug.

On 30 Jun 2014 (Day 109, 45 days after the last dose), the subject died and it was unknown if the death was due to disease progression.

Subject Number	16031012
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-015547
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Jaundice

A 55-year-old white female was diagnosed with hepatocellular carcinoma on 10 Dec 2013. Significant medical history included cholecystectomy, cholelithiasis, chronic hepatitis B, hypertension, increased gamma-glutamyltransferase, supraventricular arrhythmia, and postmenopause. Previous anticancer therapies included transcatheter arterial chemoembolization (3x). Prior and concomitant medications included bisoprolol, enoxaparin, furosemide, losartan, methylprednisolone propranolol, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe; duodenum hepatis, para-aortic, and para-caval lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 25 Aug 2014 (Day 132), the subject experienced skin exfoliation (exfoliation of foot skin; Grade 2). On 26 Aug 2014 (Day 133), the study drug dose was interrupted due to skin exfoliation. On 29 Aug 2014 (Day 136), the study drug was resumed at same dose. On 11 Sep 2014 (Day 149), the subject recovered from skin exfoliation. On 26 Sep 2014 (Day 164), the subject again experienced another episode of skin exfoliation (Grade 2) and on 27 Sep 2014 (Day 165), the study drug dose was interrupted due to this event. On 03 Oct 2014 (Day 171), the study drug was resumed at same dose. On 09 Oct 2014 (Day 177), the subject recovered from skin exfoliation. The Investigator considered skin exfoliation nonserious and possibly related to the study drug.

On 23 Mar 2016 (Day 708), the subject was hospitalized for jaundice (Grade 3). Ultrasound of abdomen showed no signs of dilatation of bile ducts; CT scan of abdomen showed stable disease with increased cirrhosis. Laboratory tests showed ALP 379 U/L (NR: 30 – 120), ALT 292 U/L (NR: 0 – 35), AST 372 U/L (NR: 0 – 35), and total bilirubin 100.2 umol/L (NR: 5 – 21). On the same day (Day 708), the study drug was interrupted due to jaundice. On 24 Mar 2016 (Day 709), laboratory tests showed hepatitis B surface antibody negative, hepatitis B core antibody positive, positive hepatitis B DNA assay, hepatitis C antibody negative, HIV antibody negative, and HIV antigen negative. On 25 Mar 2016 (Day 710), the severity of jaundice improved to Grade 2. On 26 Mar 2016 (Day 711), the subject was discharged from hospital. The subject did not recover from jaundice. The Investigator considered jaundice serious and not related to the study drug but related to disease progression.

On 13 May 2016 (Day 759), the severity of jaundice worsened to Grade 4 and the subject also experienced peripheral edema (Grade 2). A CT scan of the abdomen showed disease progression with a lymph node obstructing common bile duct. Laboratory tests showed AST 275 U/L, ALT 109 U/L, ALP 391 U/L, total bilirubin 283.8 umol/L, and albumin 26.6 g/L (NR: 35 – 52).

On 07 Jun 2016 (Day 784), the subject was hospitalized for jaundice (Grade 3) and also experienced portal vein thrombosis (Grade 2). The subject underwent curative endoscopic retrograde cholangiopancreatography. The subject was treated with enoxaparin, furosemide, and spironolactone. On the same day (Day 784), the severity of peripheral edema improved to Grade 1. On 25 Aug 2016 (Day 863), the subject recovered from jaundice. The subject did not recover from portal vein thrombosis and peripheral edema. The Investigator considered jaundice serious and not related to the study drug but related to disease progression; portal vein thrombosis and peripheral edema nonserious and not related to the study drug, but related to disease progression.

On 09 Jun 2016 (Day 786), the subject was withdrawn from study due to disease progression. The subject received the last dose of the study drug on 22 Mar 2016 (Day 707).

Subject Number	16031014
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000626
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Perineal abscess

A 67-year-old white male was diagnosed with hepatocellular carcinoma on 20 May 2014. Significant medical history included coronary arterial stent insertion, hypertension, arteriosclerosis (atherosclerotic coronary disease), congestive cardiomyopathy, laryngeal cancer, lipid metabolism disorder, type 2 diabetes mellitus, and hepatic steatosis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included acetylsalicylic acid, carvedilol, cilazapril, clemastine, glimepiride, nystatin, pantoprazole, and tocanol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes; bilateral mediastinal, bilateral iliac, bilateral axillary, celiac artery, celiac, para-caval, porta-hepatis, and right supraclavicular lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 07 Jul 2014 (Day 1), treatment with study drug was initiated.

On 01 Oct 2014 (Day 87), the subject was hospitalized for perineal abscess (Grade 3) and the study drug was interrupted. Laboratory tests showed CRP 49.959 mg/L (NR: 0 – 5) and WBC 11.4 x10^9/L (NR: 4 – 10.5). The subject underwent abscess drainage. On 03 Oct 2014 (Day 89), the subject recovered from this event. On 08 Oct 2014 (Day 94), the study drug was resumed at same dose. The Investigator considered perineal abscess serious and not related to the study drug.

On 04 Mar 2015 (Day 241), tumor response assessment showed disease progression, however the scans of 07 Jan 2015 (Day 185) were initially assessed as stable disease and later on 14 Dec 2015 (Day 526) were re-evaluated as disease progression. The subject was withdrawn from study due to disease progression. The subject received the last dose of study drug on 03 Mar 2015 (Day 240).

On 25 Aug 2015 (Day 415, 175 days after the last dose), the subject died due to disease progression.

Subject Number	16031024
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-008654
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Pathological fracture, Atrial flutter

A 64-year-old white male was diagnosed with hepatocellular carcinoma on 26 Mar 2015. Significant medical history included diabetes mellitus, cardiac failure, esophageal varices, hypertension, cancer pain (lower left limb metastases), gastritis, goiter, obesity, atrial fibrillation, coronary arterial stent insertion (diagonal artery and posterior descending artery), coronary artery disease, and hepatic steatosis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amlodipine, ascorbic acid w/minerals, atorvastatin, bisoprolol, carvedilol, dexamethasone, enoxaparin, indapamide, human insulin, magnesium sulfate, metoprolol, other combinations of nutrients (Na+, K+, Ca2+, Cl, CH3COO, and C6H5O73), potassium, targin, and valsartan. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes; masses at lumbar vertebrae, multiple sites of pelvis, multiple sites of rib. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 11 Jun 2015 (Day 1), treatment with study drug was initiated.

On 12 Jun 2015 (Day 2), the subject experienced cancer pain (worsening metastatic left lower limb pain; Grade 3). Treatment included targin. On 10 Jul 2015 (Day 30), the study drug was interrupted due to this event. The subject was recovering from cancer pain. The Investigator considered cancer pain nonserious and not related to the study drug.

On 26 Jun 2015 (Day 16), the subject experienced pain in extremity (Grade 2) with deterioration in the general condition due to left lower limb pain. On 13 Jul 2015 (Day 33), the subject recovered from pain in extremity. The Investigator considered pain in extremity nonserious and not related to the study drug.

On 13 Jul 2015 (Day 33), the subject was hospitalized for pathological fracture (malignant pubic bone fracture; Grade 2). The subject was treated with palliative radiotherapy. On 15 Jul 2015 (Day 35), the study drug was resumed at the same dose. On 16 July 2015 (Day 36), computerized tomography scan of abdomen and pelvis confirmed metastatic foci in the pelvic bones and pubic bone fracture. On 17 Jul 2015 (Day 37), the subject was discharged. The subject did not recover from pathological fracture. The Investigator considered pathological fracture serious and not related to the study drug.

On 12 Aug 2015 (Day 63), electrocardiogram showed atrial flutter (Grade 3) and was subsequently hospitalized for the event with heart rate 150 bpm, and the study drug was interrupted due to this event. Laboratory tests showed normal results. The subject was treated with enoxaparin, other combinations of nutrients (Na+, K+, Ca2+, Cl CH3COO, and C6H5O73), magnesium sulfate, metoprolol, indapamide, bisoprolol, ascorbic acid w/minerals, and

potassium. On the same day (Day 63), the subject recovered from atrial flutter and was discharged from the hospital. The Investigator considered atrial flutter serious and not related to the study drug.

On 19 Aug 2015 (Day 70), tumor response assessment showed disease progression. On 26 Aug 2015 (Day 77), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on 12 Aug 2015 (Day 63).

On 22 Dec 2015 (Day 195, 132 days after the last dose), the subject died due to unknown cause.

Subject Number	17011004
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-010655
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Pathological fracture

A 42-year-old white female was diagnosed with hepatocellular carcinoma on 07 Apr 2015. Significant medical history included arthralgia (hip pain) and insomnia. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amitriptyline, avena sativa, chlorphenamine, codeine, cyclizine, diazepam, diclofenac, loperamide, morphine, naproxen, omeprazole, other emollients and protectives (udderly cream), oxycodone, paracetamol, vitamin b complex, zoledronic acid, and zopiclone. At Screening, tumor assessments of target/non-target lesions via CT scan showed mass at left pelvis and soft tissue mass in ventral left neck. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 28 Apr 2015 (Day 1), treatment with study drug was initiated.

On 30 Apr 2015 (Day 3), the subject experienced fatigue (Grade 3). On 07 May 2015 (Day 10), the subject experienced rash (Grade 3) and erythema (erythema on face and neck; Grade 2). The subject was treated with avena sativa, chlorphenamine, and other emollients and protectives (udderly cream). On 10 May 2015 (Day 13), the study drug was interrupted due to rash. On 11 May 2015 (Day 14), the study drug remained interrupted due to fatigue. On 12 May 2015 (Day 15), the severity of rash improved to Grade 1. On 18 May 2015 (Day 21), the study drug was resumed at a reduced dose of 400 mg/day due to rash. On 29 May 2015 (Day 32), the severity of erythema improved to Grade 1. On 01 Jun 2015 (Day 35), the severity of fatigue improved to Grade 1. On 15 Jun 2015 (Day 49), the subject recovered from rash. The subject did not recover from fatigue and erythema. The Investigator considered fatigue, rash, and erythema nonserious and probably related to the study drug.

On 11 Sep 2015 (Day 137), the subject experienced arthralgia (worsened left hip pain; Grade 2). On 17 Sep 2015 (Day 143), the subject was hospitalized for pathological fracture (left acetabular undisplaced pathological fracture; Grade 3) which was confirmed by CT scan and MRI of pelvis. Treatment included morphine, codeine, paracetamol, and oxycodone. On 26 Oct 2015 (Day 182), the study drug was interrupted due to pathological fracture and the subject underwent hip arthroplasty. The subject recovered from pathological fracture event on the same day (Day 182). On 30 Oct 2015 (Day 186), the study drug was resumed at same dose. The subject did not recover from arthralgia. The Investigator considered pathological fracture serious and not related to the study drug but related to disease progression; arthralgia nonserious and not related to the study drug but related to disease progression.

On 01 Feb 2016 (Day 280), tumor response assessment showed disease progression. On 15 Feb 2016 (Day 294), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on the same day (Day 294).

Subject Number	17021001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01554-CLI-GB
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Hypoglycaemia, Hypotension, Dyspnoea, Diabetic foot infection

A 64-year-old white male was diagnosed with hepatocellular carcinoma on 17 Mar 2014. Significant medical history included alcoholic cirrhosis, cough, Dupuytren's contracture, dyspnea, hemochromatosis, hypertension, decreased appetite, palmar erythema, productive cough, type 2 diabetes mellitus, tympanic membrane perforation, and weight decreased. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included antibiotics (unknown), bendroflumethiazide, clarithromycin, clotrimazole, doxycycline, enoxaparin, flucloxacillin, insulin lispro, loperamide, metformin, metoclopramide, metronidazole, omeprazole, potassium-sandoz, prednisolone, ramipril, and simvastatin. At Screening, tumor assessments of target/non-target lesions via CT scan showed epigastric, porta-hepatis, celiac axis, para-aortic and retrocrural lymphadenopathies; bilateral pleural effusion. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

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

On 17 Jul 2014 (Day 31), the subject experienced diabetic foot (ulcer, plantar aspect right foot; Grade 2). On 12 Sep 2014 (Day 88) the subject was hospitalized for diabetic foot infection (Grade 3). On the same day (Day 88), the study drug was interrupted due to diabetic foot infection. The x-ray of right foot ruled out osteomyelitis. Wound culture was positive for Group B Streptococcus. The subject was treated with flucloxacillin, unknown antibiotics, and metronidazole. On 06 Oct 2014 (Day 112), the subject recovered from diabetic foot infection, but did not recover from diabetic foot (ulcer). The Investigator considered diabetic foot infection serious and not related to study drug; diabetic foot nonserious and not related to the study.

On 20 Jul 2014 (Day 34), the subject was hospitalized for hypoglycemia (Grade 1) with glucose 4.3 mmol/L (Normal range not provided). On the same day (Day 34), the study drug was interrupted due to this event and the dose of insulin lispro was reduced. On 21 Jul 2014 (Day 35), the study drug was resumed at same dose. On 22 Jul 2014 (Day 36), the subject recovered from hypoglycemia. The Investigator considered hypoglycemia serious and not related to study drug.

On 12 Aug 2014 (Day 57), the subject was hospitalized for dyspnea (Grade 3) and hypotension (Grade 3) with blood pressure of 99/57 mmHg. The subject was treated with prednisolone and doxycycline. On the same day (Day 57), the study drug was interrupted due to dyspnea and hypotension. On 13 Aug 2014 (Day 58), the subject recovered from hypotension. On 15 Aug 2014 (Day 60), computerized tomography scan of the thorax showed bilateral pleural effusions and new basal lung fibrosis. On 19 Aug 2014 (Day 64), the study drug was resumed at same dose. On 21 Aug 2014 (Day 66), the subject recovered from dyspnea. The Investigator considered hypotension and dyspnea serious and not related to study drug.

On 21 Oct 2014 (Day 127), the subject was withdrawn from the study per Investigator's decision. The subject received the last dose of study drug on 11 Sep 2014 (Day 87).

On 12 Nov 2014 (Day 149), tumor response assessment showed disease progression.

On 18 Dec 2014 (Day 185, 98 days after the last dose), the subject died due to disease progression.

Subject Number	17021002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001937
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Malignant ascites, Anaemia, Abdominal pain

A 70-year-old-white male was diagnosed with hepatocellular carcinoma on 18 Jun 2014. Significant medical history included alcohol abuse, appendectomy, back pain, bilateral palmar erythema, hepatic cirrhosis, esophageal variceal ligation, electrocardiogram QT prolonged, tuberculosis, vasectomy, and decreased weight. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amlodipine, avena sativa, lansoprazole, loperamide, metoclopramide, panadeine co, propranolol, stomatologicals, mouth preparations, thiamine, and vitamin b complex. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, right adrenal mass, and ascites. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 02 Sep 2014 (Day 1), treatment with study drug was initiated.

On 29 Oct 2014 (Day 58), tumor response assessment showed disease progression. On 06 Nov 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 the same day (Day 66).

On 19 Nov 2014 (Day 79), the subject was hospitalized for abdominal pain (Grade 2), anemia (Grade 3), and malignant ascites (Grade 3). Laboratory tests showed RBC 2.91 x10^12/L (NR: 4.5 – 6.5), Hct 0.235 L/L (NR: 0.4 – 0.54), and Hgb 79 g/L (NR: 135 – 180). Abdominal ultrasound showed ascites and abdominal paracentesis was performed. The subject was transfused with two units of packed red blood cells. On 20 Nov 2014 (Day 80), the subject recovered from malignant ascites. On 24 Nov 2014 (Day 84), the subject recovered from abdominal pain. The subject did not recover from anemia. The Investigator considered abdominal pain and malignant ascites serious and not related to study drug but related to disease progression; anemia serious and not related to study drug.

On 17 Dec 2014 (Day 107, 41 days after the last dose), the subject died due to disease progression.

Subject Number	17021008
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-013146
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Oesophageal varices haemorrhage

A 69-year-old white male was diagnosed with hepatocellular carcinoma on 26 Aug 2014. Significant medical history included alcohol abuse, ascites, hepatic cirrhosis, palmar erythema, spider nevus, back pain, Dupuytren's contracture, hypertension, type 2 diabetes mellitus, and spinal operation (spinal stenosis surgery). The subject did not receive any previous anticancer therapies. Prior and concomitant medications included acetylsalicylic acid, amlodipine, bactrim, folic acid, furosemide, lekovit ca, ramipril, simvastatin, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe and porta-hepatis lymphadenopathy. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 29 Apr 2015 (Day 1), treatment with study drug was initiated.

On 02 Jun 2015 (Day 35), the subject experienced decreased appetite (Grade 1) and lethargy (Grade 1). On 23 Jun 2015 (Day 56), event of lethargy worsened to (Grade 2). On 19 Aug 2015 (Day 113), the subject's decreased appetite worsened to Grade 3. No treatment was provided. On 15 Sep 2015 (Day 140), the study drug was interrupted due to lethargy and decreased appetite. On 22 Sep 2015 (Day 147), the severity of decreased appetite improved to Grade 1. On the same day (Day 147), the subject also experienced diarrhea (Grade 1). On the same day (Day 147), the study drug was resumed at a reduced dose of 400 mg/day due to decreased appetite and lethargy. The subject was recovering from decreased appetite. The subject did not recover from lethargy, and diarrhea. The Investigator considered lethargy and diarrhea nonserious and probably related to the study drug; decreased appetite nonserious and possibly related to the study drug.

On 24 Nov 2015 (Day 210), the subject's diarrhea worsened to Grade 2. No treatment was provided. On 04 Dec 2015 (Day 220), tumor response assessment showed disease progression. On 08 Dec 2015 (Day 224), the study drug was interrupted due to diarrhea. On the same day (Day 224), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 07 Dec 2015 (Day 223). The subject did not recover from diarrhea. The Investigator considered diarrhea nonserious and possibly related to the study drug.

On 22 Dec 2015 (Day 238), the subject was hospitalized for esophageal varices hemorrhage (Grade 2). The subject underwent esophagogastroduodenoscopy with variceal banding. On 31 Dec 2015 (Day 247), the subject recovered from esophageal varices hemorrhage. The Investigator considered esophageal varices hemorrhage serious and not related to the study drug.

Subject Number	17041001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01551-CLI-GB
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Pneumonia, Biliary tract infection
AE(s) Leading to Discontinuation	Pneumonia

A 75-year-old white male was diagnosed with hepatocellular carcinoma on 20 May 2014. Significant medical history included hypertension, nonalcoholic steatohepatitis, and polymyalgia rheumatica. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amoxicillin, bendroflumethiazide, cetirizine, clarithromycin, codeine, cyclizine, ertapenem, lactulose, lansoprazole, loperamide, metoclopramide, prednisolone, sertraline, simvastatin, spironolactone, trimethoprim, and zopiclone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right lobes of liver; lymphadenopathy between portal vein and inferior vena cava. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 04 Aug 2014 (Day 27), the subject was hospitalized for pneumonia (Grade 3) with temperature of 39.5 °C. Chest x-ray showed left basal consolidation, effusion, and pneumonia. The subject was treated with ertapenem, clarithromycin, and amoxicillin. On 04 Aug 2014 (Day 27), the subject was withdrawn from the study due to pneumonia and received the last dose of study drug on the same day. On 05 Aug 2014 (Day 28), the subject experienced abdominal discomfort (right upper quadrant; Grade 2), nausea (Grade 1), pyrexia (Grade 1), and fatigue (Grade 2). The subject was treated with cyclizine. On 11 Aug 2014 (Day 34), the subject recovered from pneumonia and pyrexia, and was discharged from the hospital. The subject did not recover from nausea, fatigue, and abdominal discomfort. The Investigator considered pneumonia serious and not related to study drug; nausea nonserious and possibly related to study drug; pyrexia, abdominal discomfort, and fatigue nonserious and not related to study drug.

On 15 Aug 2014 (Day 38), the subject was hospitalized for biliary tract infection (Grade 3) and was treated with clarithromycin, codeine, and zopiclone. Laboratory test showed total bilirubin 47 umol/L (NR: 0 – 21). On 19 Aug 2014 (Day 42), the subject recovered with sequelae from biliary tract infection and was discharged from the hospital. The Investigator considered biliary tract infection serious and not related to study drug.

On 03 Sep 2014 (Day 57), tumor response assessment showed disease progression.

On 19 Sep 2014 (Day 73, 46 days after the last dose), the subject died due to disease progression.

Subject Number	17041008
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-005848
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Gastroenteritis

A 61-year-old white male was diagnosed with hepatocellular carcinoma on 27 Aug 2014. Significant medical history included ascites, constipation, gout, hepatic cirrhosis, increased blood cholesterol, hypothyroidism, non-alcoholic steatohepatitis, and type 2 diabetes mellitus. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included acetylsalicylic acid, allopurinol, carvedilol, codeine, electrolytes w/macrogol, ezetimibe, furosemide, lactulose, loperamide, metformin, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at 4, 5, and 8 segments of liver; large node anterior to inferior vena cava (IVC), numerous retroperitoneal, para-aortic, and aortocaval lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

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

On 01 Apr 2015 (Day 132), the subject experienced gastroenteritis (Grade 3), flatulence (Grade 1), and diarrhea (Grade 2) which was ongoing since 01 Mar 2015 (Day 101) as Grade 1. The subject was treated with loperamide and codeine. On 06 Apr 2015 (Day 137), the subject was hospitalized for gastroenteritis and was treated with intravenous fluids. On 07 Apr 2015 (Day 138), the study drug was interrupted due to gastroenteritis. On the same day (Day 138), the subject recovered from gastroenteritis with sequelae, and recovered from flatulence and was discharged from the hospital. On 10 Apr 2015 (Day 141), the subject recovered from diarrhea. On 13 Apr 2015 (Day 144), the study drug was resumed at same dose. The Investigator considered gastroenteritis serious and not related to the study drug; diarrhea nonserious and possibly related to the study drug; flatulence nonserious and not related to the study drug.

On 08 May 2015 (Day 169), tumor scans were initially assessed as stable disease and later on 21 Aug 2015 (Day 274), were re-evaluated as disease progression.

On 03 Jul 2015 (Day 225), tumor response assessment showed disease progression. On 31 Jul 2015 (Day 253), the subject was withdrawn from study due to disease progression and received the last dose of study drug on the same day (Day 253).

Subject Number	17041014
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-018330
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Confusional state

A 62-year-old white male was diagnosed with hepatocellular carcinoma on 13 Nov 2014. Significant medical history included diabetes mellitus, hepatic cirrhosis, hepatitis B virus test positive, hypertension, drug hypersensitivity to penicillin, and portal hypertension. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included ascorbic acid w/biotin/calcium chloride/calcium pantothenate, carvedilol, entecavir, furosemide, lisinopril, magnesium, metronidazole, novomix, and spironolactone. 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 0, and Child Pugh score was 5.

On 24 Jul 2015 (Day 1), treatment with study drug was initiated.

On 08 Jan 2016 (Day 169), the subject experienced diarrhea (Grade 1) and was treated with metronidazole. On 22 Jun 2016 (Day 335), the study drug dose was reduced to 600 mg/day due to the persisting nature of ongoing diarrhea. On 02 Jul 2016 (Day 345), the subject was hospitalized for confusional state (Grade 3), hypokalemia (Grade 3), and was treated with potassium. Sodium level was within normal limits. On 09 Jul 2016 (Day 352), the subject recovered from confusional state and hypokalemia. On 19 Aug 2016 (Day 393), the subject recovered from diarrhea. The Investigator considered confusional state serious and possibly related to study drug; diarrhea nonserious and probably related to the study drug; hypokalemia nonserious and possibly related to study drug.

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

Subject Number	18041002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01522-CLI-DE
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Gastric haemorrhage (2x), Lung infection

A 71-year-old white male was diagnosed with hepatocellular carcinoma on 18 Feb 2010. Significant medical history included hypertension, metastases to bone, cholecystectomy, turbinectomy, diabetes mellitus, fatigue intermittent, hepatitis B, sleep apnea syndrome, abdominal pain, back pain, benign prostatic hyperplasia, and thyroidectomy. Previous anticancer therapies included radiotherapy to right side of shoulder, hepatectomy (liver segment IV), and radiofrequency ablation. Prior and concomitant medications included adefovir, amlodipine, buprenorphine, clarithromycin, dalteparin, enemas, floradix, gadoteric acid, hydrochlorothiazide, hydromorphone, iomeprol, iron, kalinor-acid, lactulose, lamivudine, levothyroxine, loperamide, metformin, metoclopramide, mometasone, novo-petrin, pantoprazole, propofol, ramipril, sitagliptin, unacid, urea, vitamin B complex, and zoledronic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left lobe of liver, soft tissue mass in right side of diaphragm, right upper lobe of lung and lung masses. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 02 Apr 2014 (Day 1), treatment with study drug was initiated.

On 07 Jun 2014 (Day 67), the subject experienced gastric hemorrhage (Grade 2) and was hospitalized on 10 Jun 2014 (Day 70) for worsening gastric hemorrhage (Grade 3). The subject also experienced anemia (Grade 2) and gastric ulcer (Grade 3). The study drug was interrupted due to gastric hemorrhage. Gastroscopy showed gastric ulcer in corpus ventriculi and two clips were placed on the peptic ulcer. Laboratory tests showed RBC 3.06 x10^12/L (NR: 4.2 – 5.6) and Hgb 96 g/L (NR: 135 – 175). Treatment included packed RBC transfusion, pantoprazole, propofol, and novo-petrin. On 12 Jun 2014 (Day 72), the subject recovered from gastric hemorrhage. On the same day (Day 72), the subject experienced lung infection (Grade 2) and chest x-ray showed infiltrates. Laboratory tests showed WBC 8.33 x10^9/L (NR: 3.5 – 10), absolute neutrophil count 10.92 x10^9/L (NR: 1.5 – 7.5), and CRP 219 mg/L (NR: 0 – 5). The subject was treated with clarithromycin and unacid. On 16 Jun 2014 (Day 76), the subject recovered from lung infection. On 24 Jun 2014 (Day 84), the study drug was resumed at the same dose. The subject did not recover from gastric ulcer and anemia. The Investigator considered gastric hemorrhage serious and possibly related to the study drug; lung infection serious and not related to the study drug; anemia and gastric ulcer nonserious and not related to the study drug.

On 04 Jul 2014 (Day 94), the subject was hospitalized for gastric hemorrhage (Grade 3) with gastroscopy showing an ulcer of corpus ventriculi and the severity of anemia worsened to Grade 3. Laboratory tests showed Hgb 62 g/L, Hct 0.199 L/L (NR: 0.39 – 0.49), and RBC 2.11 x10^12/L. On 04 Jul 2014 (Day 94), the study drug was interrupted due to gastric hemorrhage. On 07 Jul 2014 (Day 97), the subject recovered from gastric hemorrhage and the

study drug was resumed at the same dose. The subject did not recover from anemia. The Investigator considered gastric hemorrhage serious and possibly related to the study drug; anemia nonserious and not related to the study drug.

On 23 Jul 2014 (Day 113), tumor response assessment showed disease progression. On 19 Aug 2014 (Day 140), the subject was withdrawn from the study due to disease progression. The subject received the last dose of the study drug on the same day (Day 140).

On 02 May 2015 (Day 396, 256 days after the last dose), the subject died due to disease progression.

Subject Number	18081005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000826
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Ascites

A 62-year-old white male was diagnosed with hepatocellular carcinoma on 04 Feb 2014. Significant medical history included back pain, gastroesophageal reflux disease (grade b), hepatitis C, headache (intermittent), insomnia, hyperthyroidism (latent), and hepatic cirrhosis. Previous anticancer therapy included transcatheter arterial chemoembolization (4x). Prior and concomitant medications included hydromorphone, loperamide, metamizole, pantoprazole, and zopiclone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes; and mass at right lobe of lung. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 18 Sep 2014 (Day 57), tumor response assessment showed disease progression and the subject was withdrawn from the study due to disease progression. The subject received the last dose of the study drug on 17 Sep 2014 (Day 56).

On 30 Sep 2014 (Day 69), the subject was hospitalized for ascites (abdominal pain due to ascites of unknown etiology; Grade 3) and also had portal vein thrombosis (Grade 2) confirmed by ultrasound of abdomen. Laboratory tests showed albumin 28.9 g/L (NR: 35 – 42), ALT 68 U/L (NR: 0 – 45), AST 205 U/L (NR: 0 – 35), ALP 216 U/L (NR: 40 – 129), INR 1.08 (NR: 0.8 – 1.2), PT 34.4 sec (NR: 0 – 21), and total bilirubin 17.1 umol/L (NR: 0 – 17.1). On 01 Oct 2014 (Day 70), abdominal cavity drainage was performed. On 02 Oct 2014 (Day 71), the subject recovered with sequelae from ascites and portal vein thrombosis. The Investigator considered ascites serious and not related to study drug but related to disease progression; portal vein thrombosis nonserious and not related to study drug.

On 13 Dec 2014 (Day 143, 87 days after the last dose), the subject died and the cause of death was not disease progression.

Subject Number	19011005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-006762
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Acute sinusitis

A 74-year-old white female was diagnosed with hepatocellular carcinoma on 13 Feb 2014. Significant medical history included erosive gastritis, chronic gastritis, chronic hepatitis B, hepatitis D, chronic pancreatitis, hepatic cirrhosis, rectal fistula repair, coronary artery disease, abdominal discomfort, hypertension, osteoarthritis (knee), portal hypertension, and tonsillectomy. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amlodipine, betamethasone, captopril, cefazolin, cefixime, ciprofloxacin, cyanocobalamin, dexamethasone, enalapril, entecavir, furosemide, general nutrients, glycyrrhizic acid, indapamide, iron, loperamide, nifedipine, spironolactone, trophicard, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes; multiple and right middle lobe lung masses; and bifurcation conglomerate lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 01 Apr 2014 (Day 2), the subject experienced hypertension (Grade 3) (Blood pressure result not provided) and was treated with amlodipine, enalapril, and nifedipine. On the same day (Day 2), the subject recovered from hypertension. On 02 Apr 2014 (Day 3), the study drug dose was reduced to 400 mg/day due to hypertension. The Investigator considered hypertension nonserious and probably related to the study drug.

On 22 Jan 2015 (Day 298), the subject experienced acute sinusitis (Grade 2) and was treated with cefixime. The subject recovered on 29 Jan 2015 (Day 305). The Investigator considered acute sinusitis nonserious and not related to the study drug.

On 06 May 2015 (Day 402), the subject was hospitalized for acute sinusitis (Grade 2). Face and mouth x-ray showed clear decrease of maxillary and frontal sinuses. The subject was treated with cefazolin, ciprofloxacin, and dexamethasone. On the same day (Day 402), the study drug was interrupted due to acute sinusitis. On 20 May 2015 (Day 416), the subject recovered from acute sinusitis. On 28 May 2015 (Day 424), the study drug was resumed at the same dose. The Investigator considered acute sinusitis serious and not related to the study drug.

On 13 Jan 2016 (Day 654), tumor response assessment showed disease progression. On 18 Jan 2016 (Day 659), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on the same day (Day 659).

Subject Number	19011010
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-003330
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Duodenal ulcer haemorrhage, Hepatic failure

A 57-year-old white male was diagnosed with hepatocellular carcinoma on 06 May 2014. Significant medical history included arteriosclerosis (aorta and coronary atherosclerosis), hypertension, cholelithiasis, duodenitis, hemorrhoids, hepatic cirrhosis, large intestine polyp, peptic ulcer of duodenum, myocardial ischemia, left adrenal gland adenoma, and subacute conjunctivitis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included ademetionine, amlodipine, bismuth, bisoprolol, captopril, dexamethasone, drotaverine, enalapril, ginkgo biloba, iron, nifuroxazide, omeprazole, ornithine, rabeprazole, simeticone, troxerutin, and ursodeoxycholic acid. 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 21 May 2014 (Day 1), treatment with study drug was initiated.

On 17 Jun 2014 (Day 28), the subject experienced hypertension (Grade 3). Blood pressure was not provided and the subject was treated with captopril. The subject recovered from hypertension on the same day (Day 28). On 18 Jun 2014 (Day 29), blood pressure was 125/84 mmHg and the study drug dose was reduced to 400 mg/day due to hypertension. The Investigator considered hypertension nonserious and probably related to the study drug.

On 25 Nov 2014 (Day 189), the subject had abdominal pain (Grade 2). The subject was treated with drotaverine, nifuroxazide, and simeticone. On 30 Dec 2014 (Day 224), the subject experienced melena and hematemesis. On the same day (Day 224), the subject was hospitalized for duodenal ulcer hemorrhage (Grade 4) confirmed by upper gastrointestinal tract endoscopy. Treatments included bismuth and blood transfusion. On 31 Dec 2014 (Day 225), the study drug was interrupted due to duodenal ulcer hemorrhage. On 12 Jan 2015 (Day 237), the subject recovered from duodenal ulcer hemorrhage and was discharged from the hospital. On 22 Jan 2015 (Day 247), the subject experienced hemorrhagic anemia (Grade 2) with Hgb 87.6 g/L (NR: 120 – 180) and was treated with iron and omeprazole. On 26 Jan 2015 (Day 251), repeat upper gastrointestinal tract endoscopy did not show duodenal ulcer with bleeding. On 10 Feb 2015 (Day 266), the subject recovered from abdominal pain. On 18 Feb 2015 (Day 274), the subject recovered from hemorrhagic anemia with Hgb 115 g/L (NR: 130 – 165). On 26 Feb 2015 (Day 282), the study drug was resumed at same dose. The Investigator considered duodenal ulcer hemorrhage serious and possibly related to the study drug; abdominal pain nonserious and probably related to the study drug; hemorrhagic anemia nonserious and not related to the study drug.

On 05 Nov 2015 (Day 534), the subject experienced increased blood bilirubin (Grade 2) with total bilirubin 42.1 umol/L (NR: 0 – 18.8). On the following day (Day 535), the study drug was

interrupted due to this event and the subject was treated with ademetionine and ornithine. The subject did not recover from increased blood bilirubin. The Investigator considered increased blood bilirubin nonserious and probably related to the study drug.

On 03 Dec 2015 (Day 562), the subject experienced increased gamma-glutamyltransferase (Grade 4) which started as Grade 3 on 13 Aug 2014 (Day 85). On the same day (Day 562), the subject was diagnosed with hepatic failure (Grade 3) and was admitted to the hospital on 07 Dec 2015 (Day 566) for further evaluation. Laboratory tests showed GGT 1350 U/L (NR: 10 – 49), ALP 440 U/L (NR: 43 – 115), AST 243 U/L (NR: 10 – 43), ALT 68 U/L (NR: 10 – 40), and total bilirubin 46.9 umol/L. The subject was treated with ornithine. On 03 Dec 2015 (Day 562), tumor response assessment showed disease progression. On 09 Dec 2015 (Day 568), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 05 Nov 2015 (Day 534). On 05 Jan 2016 (Day 595, 61 days after the last dose), the subject died due to hepatic failure. Autopsy was not performed. At the time of death, the subject had not recovered from increased gamma-glutamyltransferase. The Investigator considered hepatic failure serious and possibly related to the study drug and related to disease progression; increased gamma-glutamyltransferase nonserious and not related to the study drug.

Subject Number	19011023
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-009323
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Hepatic failure

A 75-year-old white male was diagnosed with hepatocellular carcinoma on 18 Oct 2013. Significant medical history included hepatitis A, appendectomy, arteriosclerosis, basal cell carcinoma (front chest), duodenitis, chronic gastritis, chronic hepatitis C, chronic prostatitis, hepatic cirrhosis, duodenal ulcer, esophageal varices, nephroptosis, skin neoplasm excision, gastric ulcer, and thrombocytopenia. Previous anticancer therapies included transcatheter arterial chemoembolization (2x). Prior and concomitant medications included ademetionine, amitriptyline, cetirizine, citicoline, diosmectite, etamsilate, fenspiride, glycyrrhizic acid, human albumin, lactobacillus acidophilus, loperamide, menadione, omeprazole, ornithine, pancreatin, pipemidic acid, propranolol, simeticone, spironolactone, tamsulosin, triderm, and ursodeoxycholic acid. 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 14 Nov 2014 (Day 1), treatment with study drug was initiated.

On 17 Nov 2014 (Day 4), the subject experienced diarrhea (Grade 1). Treatment included lactobacillus acidophilus and loperamide. On 28 Nov 2014 (Day 15), the subject experienced rash (Grade 1). On 15 Dec 2014 (Day 32), the subject experienced pruritus (Grade 2). On 29 Dec 2014 (Day 46), the subject experienced asthenia (Grade 2). On the same day (Day 46), the study drug was reduced to 400 mg/day due to persistent diarrhea, rash, pruritus, and asthenia. Treatment included loperamide, lactobacillus acidophilus, and triderm. On 20 Jul 2015 (Day 249), the subject experienced upper abdominal pain (Grade 2). On 30 Jul 2015 (Day 259), the subject experienced general weakness, diarrhea, bitter taste in the mouth, nausea, lethargy, weight loss of 7.6 kg (Baseline: 75.1 kg), and the subject was hospitalized with a diagnosis of hepatic failure (Grade 3). Laboratory tests showed AST 43.4 U/L (NR: 0 – 37), ALT 28.7 U/L (NR: 0 – 40), and albumin 34.1 g/L (NR: 35 – 50). The subject was treated with spironolactone, ornithine, and the study drug was interrupted due to ongoing pruritus, ongoing asthenia, and hepatic failure. On 04 Aug 2015 (Day 264), esophagogastroduodenoscopy showed esophageal varices (Grade 3) and portal hypertensive gastropathy (Grade 3). On 17 Aug 2015 (Day 277), the subject underwent esophageal variceal ligation. On 24 Aug 2015 (Day 284), the subject recovered from hepatic failure and was discharged from the hospital. On 26 Aug 2015 (Day 286), the subject recovered from diarrhea, pruritus, and rash. On 27 Aug 2015 (Day 287), the severity of asthenia improved to Grade 2. On 28 Aug 2015 (Day 288), the study drug was resumed at the same dose. The subject did not recover from upper abdominal pain, esophageal varices, portal hypertensive gastropathy, and asthenia. The Investigator considered hepatic failure serious and possibly related to the study drug; diarrhea nonserious and possibly related to study drug; pruritus, rash, asthenia, esophageal varices, and portal hypertensive gastropathy

nonserious and probably related to the study drug; upper abdominal pain nonserious and not related to the study drug.

On 21 Oct 2015 (Day 342), tumor response assessment showed disease progression. On 22 Oct 2015 (Day 343), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on the same day (Day 343).

Subject Number	19021037
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-015504
Assigned Treatment	Sorafenib 800 mg/day
Non-Fatal SAE(s)	Cholecystitis acute

A 75-year-old white male was diagnosed with hepatocellular carcinoma on 13 Nov 2014. Significant medical history included arteriosclerosis coronary artery, fatigue, gastritis, hepatitis B, and hypertension. Previous anticancer therapy included hepatectomy. Prior and concomitant medications included amlodipine, entecavir, losartan, and tamsulosin. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at quadrate and right liver lobes and porta-hepatis lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 10 Jul 2015 (Day 1), treatment with study drug was initiated.

On 11 Mar 2016 (Day 246), the subject was hospitalized for acute cholecystitis (Grade 3) with symptoms of pain in the right hypochondrium and nausea. On the same day (Day 246), abdominal ultrasound confirmed acute cholecystitis. On 12 Mar 2016 (Day 247), the subject underwent gallbladder puncture. On 17 Mar 2016 (Day 252), the subject recovered from the event and was discharged from the hospital. The Investigator considered acute cholecystitis serious and not related to study drug.

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