Subject Number	24111018
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001522
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Hepatic cirrhosis

A 52-year-old Chinese male was diagnosed with hepatocellular carcinoma on 02 Sep 2014. Significant medical history included hepatitis B. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included alanyl glutamine, amino acids, diosmectite, entecavir, furosemide, glucose injection, glycyrrhizic acid, lidocaine, megestrol, polyene phosphatidylcholine, retinol with tocopherol/vitamin d/vitamin k, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe, the top of liver, and right branch of portal vein. The BCLC stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 26 Sep 2014 (Day 1), treatment with study drug was initiated.

On 01 Nov 2014 (Day 37), the subject was hospitalized for hepatic cirrhosis (Grade 3). On 04 Nov 2014 (Day 40), the abdominal ultrasound showed peritoneal effusion and CT of abdomen showed liver cirrhosis, ascites, space occupying lesions in liver parenchyma, and gall bladder stones. Laboratory results showed AST 80 U/L (NR: 15 – 40), total bilirubin 27 umol/L (NR: 3.4 – 20.5), and albumin 26.3 g/L (NR: 40 – 55). The subject underwent abdominal cavity drainage and was also treated with unspecified nutritional support and unknown diuretics. The study drug dose did not change. On 13 Nov 2014 (Day 49), the subject recovered from hepatic cirrhosis. The Investigator considered hepatic cirrhosis serious and not related to the study drug.

On 15 Jan 2015 (Day 112), the tumor response assessment showed disease progression. On 21 Jan 2015 (Day 118), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on the same day (Day 118).

Subject Number	24111022
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-006059
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Jaundice cholestatic
AE(s) Leading to Discontinuation	Jaundice cholestatic

A 65-year-old Chinese female was diagnosed with hepatocellular carcinoma on 03 Sep 2014. Significant medical history included cholelithiasis. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included aceglutamide, ademetionine, azintamide, carbohydrates w/electrolytes, ceftazidime, deproteinised calf blood injection (blood, calf, deprot., lmw portion), esomeprazole, furosemide, glycyrrhizic acid, human albumin, multitrace, octreotide, polyene phosphatidylcholine, promethazine, ribonucleic acid, and thymalfasin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver and a lymph node next to gallbladder. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 26 Mar 2015 (Day 167), the subject experienced increased blood bilirubin (Grade 2) with total bilirubin 49.8 umol/L (NR: 0 – 18.8). The subject was treated with polyene phosphatidylcholine and ademetionine. On 16 Apr 2015 (Day 188), the subject experienced cholestatic jaundice (Grade 4) and a CT of abdomen showed dilation of intrahepatic bile duct. Laboratory tests showed ALP 349 U/L (NR: 50 – 135), AST 110 U/L (NR: 13 – 35), ALT 58 U/L (NR: 4 – 40), and total bilirubin 121.9 umol/L (NR: 3.4 – 20.5). On 16 Apr 2015 (Day 188), tumor response assessment showed disease progression. On 17 Apr 2015 (Day 189), the subject was withdrawn from study due to disease progression and received the last dose of the study drug on 16 Apr 2015 (Day 188). On 17 Apr 2015 (Day 189), the increased blood bilirubin worsened to Grade 3. Repeat laboratory tests showed total bilirubin 132.2 umol/L (NR: 0 – 18.8), ALP 338 U/L (NR: 30 – 115), AST 103 U/L (NR: 10 – 36), ALT 50 U/L (NR: 10 – 33), and GGT 123 U/L (NR: 5 – 32). On 18 Apr 2015 (Day 190), the subject was hospitalized for cholestatic jaundice and was treated with aceglutamide, ademetionine, human albumin, deproteinised calf blood, carbohydrates w/electrolytes, ceftazidime, esomeprazole, furosemide, glycyrrhizic acid, multitrace, octreotide, promethazine, and ribonucleic acid. On 21 Apr 2015 (Day 193), the subject underwent ultrasound-guided bile duct stent insertion. On 23 Apr 2015 (Day 195), repeat total bilirubin was 117.7 umol/L (NR: 3.4 – 20.5). On 24 Apr 2015 (Day 196), the subject recovered from cholestatic jaundice and was discharged from hospital. The outcome of increased blood bilirubin was unknown. The Investigator considered cholestatic jaundice serious and not related to the study drug but related to disease progression; increased blood bilirubin nonserious and not related to the study drug.

On 16 Jun 2015 (Day 249, 61 days after the last dose), the subject died due to disease progression.

Subject Number	24111042
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-014800
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Cerebral infarction

A 56-year-old Chinese male was diagnosed with hepatocellular carcinoma on 18 Dec 2014. Significant medical history included hepatitis B and hepatitis C. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included acetylsalicylic acid, atorvastatin, benazepril, dexamethasone, edaravone, entecavir, folic acid, indometacin, mecobalamin, nifedipine, other analgesics and antipyretics (cooling gel sheet), ozagrel, paraffin, thymalfasin, and thymostimulin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe and right branch of portal vein. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 24 Feb 2016 (Day 413), the subject was hospitalized for right hand fatigue and was diagnosed with cerebral infarction (Grade 3) confirmed by brain CT scan. On 25 Feb 2016 (Day 414), the study drug was interrupted due to this event. The subject was treated with acetylsalicylic acid, atorvastatin, edaravone, ozagrel, folic acid, and mecobalamin. On 29 Feb 2016 (Day 418), the study drug was resumed at same dose. On 25 Mar 2016 (Day 443), the subject recovered from cerebral infarction. On 13 May 2016 (Day 492), the study drug dose was reduced to 4 mg/day due to this event. The Investigator considered cerebral infarction serious and possibly related to the study drug.

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

Subject Number	24121006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-010573
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Decreased appetite
AE(s) Leading to Discontinuation	Decreased appetite

A 49-year-old Chinese male was diagnosed with hepatocellular carcinoma on 11 Oct 2010. Significant medical history included esophageal varices, cholelithiasis, hepatitis B, hepatic cirrhosis, and tuberculosis. Previous anticancer therapies included ultrasound therapy, high frequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included amoxicillin, brucea javanica, captopril, cefaclor, dexamethasone, entecavir, esomeprazole, hemocoagulase, irbesartan, ketorolac, lamivudine, megestrol, metoclopramide, mosapride, omeprazole, oxycodone, panax ginseng, pantoprazole, and unspecified herbal and traditional medicines (shenqifuzheng, weifuchun, lu gan shi xi ji, and shengmai). At Screening, tumor assessments of target/non-target lesions via CT scan showed lymphadenopathy at hilus of the lung and right mediastinum. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 19 Sep 2014 (Day 1), treatment with study drug was initiated.

On 02 Sep 2015 (Day 349), the subject was hospitalized for decreased appetite (Grade 3). The subject was treated with mosapride and megestrol. On 16 Sep 2015 (Day 363), the subject was discharged from the hospital. The study drug dose was not changed due to this event. The outcome of decreased appetite was unknown. The Investigator considered decreased appetite serious and not related to the study drug.

On 24 Jul 2015 (Day 309), the subject experienced increased gamma-glutamyltransferase (Grade 2) with GGT 141 U/L (NR: 10 – 49). On 17 Sep 2015 (Day 364), the subject experienced abnormal hepatic function (Grade 3) and increased gamma-glutamyltransferase worsened to Grade 4. Laboratory tests showed ALP 659 U/L (NR: 43 – 115), ALT 209 U/L (NR: 10 – 40), AST 340 U/L (NR: 10 – 43), total bilirubin 56.9 umol/L (NR: 0 – 18.8), and GGT 998 U/L. On 19 Sep 2015 (Day 366), the study drug was interrupted due to abnormal hepatic function. The subject did not recover from abnormal hepatic function and increased gamma-glutamyltransferase. The Investigator considered abnormal hepatic function and increased gamma-glutamyltransferase nonserious and possibly related to the study drug.

On 23 Sep 2015 (Day 370), the subject was withdrawn from study due to clinical disease progression and received the last dose of the study drug on 18 Sep 2015 (Day 365).

On 29 Nov 2015 (Day 437, 72 days after the last dose), the subject died due to disease progression. Autopsy was not performed.

Subject Number	24121007
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001479
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Diplegia
AE(s) Leading to Discontinuation	Diplegia

A 52-year-old Chinese male was diagnosed with hepatocellular carcinoma on 26 Jul 2011. Significant medical history included hepatitis B and hepatic cirrhosis. Previous anticancer therapies included microwave therapy, high frequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included adefovir, dexamethasone, enemas, entecavir, glycerol, lactulose, mannitol, morphine, oxycocet, potassium, rabeprazole, retinol w/tocopherol/vitamin D/vitamin K, thymalfasin, torasemide, unspecified herbal and traditional medicine, and vitamin b-complex with vitamin C. At Screening, tumor assessments of target/non-target lesions via CT scan showed mass at right rib; lesions at right and left portal vein, and multiple sites of liver. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 19 Sep 2014 (Day 1), treatment with study drug was initiated.

On 01 Oct 2014 (Day 13), the subject experienced hypoesthesia (lower limb numbness; Grade 1) and on 11 Oct 2014 (Day 23), the subject was hospitalized for diplegia (both lower limbs paralysis; Grade 3). On 12 Oct 2014 (Day 24), the study drug was interrupted due to diplegia. On 13 Oct 2014 (Day 25), the subject experienced anal incontinence (Grade 3) and was treated with dexamethasone and mannitol. On the same day (Day 25), the subject was withdrawn from the study due to diplegia secondary to clinical disease progression. The subject received the last dose of the study drug on 11 Oct 2014 (Day 23). On 14 Oct 2014 (Day 26), the subject experienced cancer pain (Grade 2) and started on new anticancer therapy, coix lacryma-jobi (kanglaite injection) and unspecified herbal and traditional medicine. On 15 Oct 2014 (Day 27), the subject underwent radiotherapy to the lumbar area. On 03 Nov 2014 (Day 46), the subject recovered from diplegia with sequelae. The subject did not recover from hypoesthesia and anal incontinence and it was unknown if the subject recovered from cancer pain. The Investigator considered diplegia serious and not related to the study drug but related to clinical disease progression; hypoesthesia nonserious and possibly related to the study drug; anal incontinence and cancer pain nonserious and not related to the study drug.

Subject Number	24121010
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-018245
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Jaundice cholestatic

A 47-year-old Chinese female was diagnosed with hepatocellular carcinoma on 20 Nov 2012. Significant medical history included female sterilization. Previous anticancer therapies included transcatheter arterial chemoembolization, ultrasound therapy, high frequency ablation, targeted cancer therapy (ultrasound guided soluble tumor virus injection), and radiotherapy to right liver lobe and abdominal wall. Prior and concomitant medications included antodine, captopril, cefoperazone, cefoxitin, coix lacryma-jobi, diclofenac, enalapril, levofloxacin, omeprazole, polyene phosphatidylcholine, and ribavirin. At Screening, tumor assessments of target/non-target lesions via CT scan showed masses at right lower lung lobe and bilateral lung lobes and lesion at right liver lobe. The BCLC Stage was C, ECOG performance was 0, and Child Pugh score was 5.

On 27 Nov 2014 (Day 1), treatment with study drug was initiated.

On 08 Jun 2016 (Day 560), the subject experienced abnormal hepatic function (Grade 3). Laboratory tests showed total bilirubin 9.7 umol/L (NR: 0 – 18.8), ALP 305 U/L (NR: 30 – 115), ALT 210 U/L (NR: 10 – 33), AST 182 U/L (NR: 10 – 36), and GGT 369 U/L (NR: 5 – 32). The subject was treated with polyene phosphatidylcholine. On 17 Jun 2016 (Day 569), the study drug was interrupted due to abnormal hepatic function. The subject did not recover from abnormal hepatic function. The Investigator considered abnormal hepatic function nonserious and possibly related to study drug.

On 29 Jun 2016 (Day 581), the subject was hospitalized for cholestatic jaundice (Grade 3). Laboratory tests showed total bilirubin 318.3 umol/L (NR: not provided), AST 177 U/L (NR: not provided), and ALT 165 U/L (NR: not provided). The CT scan of abdomen showed hilar cholangiocarcinoma with intrahepatic bile duct dilatation, multiple metastatic nodules in the lungs, multiple small retroperitoneal lymph nodes; right lobe atrophy with cystic lesion; pancreatic neck round point density nodules; and gallbladder wall thickening. On 30 Jun 2016 (Day 582), the subject underwent percutaneous transhepatic cholangiography and was also treated with polyene phosphatidylcholine. On 02 Jul 2016 (Day 584), the subject was discharged from the hospital. On 01 Sep 2016 (Day 645), the subject recovered from cholestatic jaundice. The Investigator considered cholestatic jaundice serious and not related to study drug.

On 22 Aug 2016 (Day 635), the subject withdrew from the study by choice. The subject received last dose of the study drug on 16 Jun 2016 (Day 568).

Subject Number	24131008
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-011763
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Spinal cord compression

A 43-year-old Chinese male was diagnosed with hepatocellular carcinoma in Aug 2012. Significant medical history included cholelithiasis, hepatitis B, pneumonia, hepatic cirrhosis, prostatic calcification, chronic gastritis, spinal cord compression (ongoing from Mar 2014), splenomegaly, renal cyst (left), and muscle atrophy (right lower limb). Previous anticancer therapies included radiotherapy to thoracic vertebral lesion, radiotherapy to right lobe liver mass, irinotecan, oxaliplatin, pirarubicin, microwave therapy, and transcatheter arterial chemoembolization. Prior and concomitant medications included adefovir, amino acids, ascorbic acid, calcium gluconate, celecoxib, decold, dexamethasone, entecavir, furosemide, general nutrients, glycerol, glycyrrhiza glabra, glycyrrhizic acid, hemocoagulase, human albumin, lactulose, levofloxacin, mannitol, mentha x piperita, mosapride, omeprazole, other drugs for disorders of the musculoskeletal system (troxerutin and cerebroprotein hydrolysate injection), paracetamol, phytomenadione, polyene phosphatidylcholine, potassium, proliv, propafenone, pyridoxine, ribonucleic acid, sodium phosphate, thymopentin, tramadol, unspecified herbal and traditional medicine (shengxuebao mixture), and zoledronic acid. At Screening, tumor assessments of target/non-target lesions via MRI showed lesion at right liver lobe, multiple sites of liver; and sacral, lumbar vertebral masses. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 16 Oct 2015 (Day 449), tumor response assessment showed disease progression. On 19 Oct 2015 (Day 452), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 18 Oct 2015 (Day 451).

On 31 Oct 2015 (Day 464), the subject experienced dysuria (Grade 1), constipation (Grade 3), peripheral edema (lower limbs) (Grade 3), and paresthesia of lower limbs (Grade 3). On 01 Nov 2015 (Day 465), the subject experienced worsening of spinal cord compression (Grade 3) and chest discomfort (Grade 1). The subject underwent bladder catheterization. On 03 Nov 2015 (Day 467), the subject was hospitalized for spinal cord compression with sensory paresthesia of lower limbs, lumbosacral tenderness, muscular power of grade 0, and hypomyotonia. The subject was treated with mannitol, dexamethasone, glycerol, lactulose, sodium phosphate, mosapride, troxerutin, and cerebroprotein hydrolysate. On 04 Nov 2015 (Day 468), MRI of spine showed hepatocellular carcinoma with bone lesion and abnormal signal in multiple vertebral body considered as a metastasis to thoracic vertebrae 4 – 5, posterior intraspinal stenosis, and spinal cord compression. On 19 Nov 2015 (Day 483), physical exam showed slightly edematous right ankle joint and reflexion had disappeared; loss of pain and temperature sensitivity but his position sense and vibration sense were intact. The subject and family requested for a discharge to a psychiatric hospital for supportive treatment. The subject

did not recover from the spinal cord compression, chest discomfort, dysuria, constipation, peripheral edema, and paresthesia. The Investigator considered spinal cord compression serious and not related to the study drug but related to disease progression; chest discomfort, peripheral edema, constipation, and paresthesia nonserious and not related to the study drug but related to disease progression; dysuria nonserious and not related to the study drug.

On 22 Feb 2016 (Day 578, 127 days after the last dose), the subject died due to disease progression.

Subject Number	24131009
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01564-CLI-CN
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Fatigue

A 74-year-old Chinese male was diagnosed with hepatocellular carcinoma on 30 Jul 2014. Significant medical history included abdominal pain, benign prostatic hyperplasia, pneumonitis, hepatitis B, hepatic cirrhosis, latent syphilis, renal cyst, and splenomegaly. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included adefovir, diisopropylamine, glutathione, levofloxacin, levoglutamide, oxycocet, pantoprazole, pyridoxine, and unspecified herbal and traditional medicine (shenmai). At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at right and left lobes of liver; portacaval space and para-aortic lymphadenopathies. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 11 Aug 2014 (Day 5), the subject stopped taking the study drug by choice.

On 21 Aug 2014 (Day 15), the subject was hospitalized for fatigue (Grade 3) which was ongoing since 04 Aug 2014 (Day –3) as Grade 1, and also experienced hepatic pain (Grade 2) which was ongoing since 30 July 2014 (Day –8) as Grade 1. Treatment given was unknown. On 23 Aug 2014 (Day 17), the subject was discharged from the hospital. On 24 Sep 2014 (Day 49), the severity of fatigue improved to Grade 2 and hepatic pain improved to Grade 1. The subject did not recover from these events. The Investigator considered fatigue serious and not related to the study drug; hepatic pain nonserious and not related to the study drug.

On 08 Oct 2014 (Day 63), the subject withdrew from the study by choice and received the last dose of study drug on 10 Aug 2014 (Day 4).

Subject Number	24131011
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01559-CLI-CN
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Hepatic pain, Pyrexia

A 40-year-old Chinese female was diagnosed with hepatocellular carcinoma on 25 Jul 2014. Significant medical history included hepatitis B and middle ear operation (left). The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amino acids with polypeptide, ascorbic acid, azintamide, ceftriaxone, celecoxib, dextrose and sodium chloride injection, diisopropylamine, entecavir, fats, fentanyl, furosemide, general nutrients (enteral nutritional powder), glutathione, glycerol, granisetron, magnesium sulfate, metoclopramide, mosapride, omeprazole, ondansetron, paracetamol, potassium, potassium magnesium aspartate, proliv, promethazine, pyridoxine, ranitidine, solutions affecting the electrolyte balance (sodium potassium magnesium calcium and glucose injection), thymopentin, tramadol, travert electrolyte No. 2, unspecified herbal and traditional medicine (danhong), and veramid. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at right liver lobe liver, multiple sites of liver, and CT scan showed multiple lung metastases. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 10 Aug 2014 (Day 3), the subject experienced hepatic pain (Grade 1) and was treated with celecoxib. On 11 Aug 2014 (Day 4), the severity of hepatic pain worsened to Grade 2 and was treated with transdermal fentanyl and tramadol. On 14 Aug 2014 (Day 7), the severity of hepatic pain worsened to Grade 3 and the subject was hospitalized. Treatment with celecoxib, transdermal fentanyl, and tramadol were continued. On 25 Aug 2014 (Day 18), the severity of hepatic pain improved to Grade 1 and the subject was discharged from the hospital. On 30 Sep 2014 (Day 54), the subject recovered from hepatic pain. The study drug dose did not change. The Investigator considered hepatic pain serious and possibly related to the study drug.

On 29 Aug 2014 (Day 22), the subject was hospitalized for pyrexia (Grade 2) with body temperature of 39.5 °C. Treatment included veramid, paracetamol, ceftriaxone, solutions affecting the electrolyte balance, and travert electrolyte No. 2. On 30 Aug 2014 (Day 23), CT scan was normal and the severity of pyrexia improved to Grade 1 with temperature of 38 °C. On 01 Sep 2014 (Day 25), the subject recovered from pyrexia. The study drug dose did not change. The Investigator considered pyrexia serious and possibly related to the study drug.

On 19 Mar 2015 (Day 224), tumor response assessment showed disease progression. On 20 Mar 2015 (Day 225), the subject was withdrawn from the study due to disease progression and the subject received the last dose of study drug on the same day (Day 225).

On 18 Jul 2015 (Day 345, 120 days after the last dose), the subject died due to disease progression.

Subject Number	24151002
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-016656
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Jaundice cholestatic
AE(s) Leading to Discontinuation	Jaundice cholestatic

A 69-year-old Chinese male was diagnosed with hepatocellular carcinoma in Dec 2010. Significant medical history included reflux gastritis, chronic gastritis, chronic hepatitis B, and hepatic cirrhosis. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included, alanyl glutamine, alprostadil, amoxicillin, anisodamine, chlorphenamine, clostridium butyricum, co-diovan, diazepam, diosmectite, entecavir, fentanyl, gabexate, glutathione, glycyrrhiza glabra, human albumin, hyoscine, iohexol, lactulose, lercanidipine, levofloxacin, loperamide, meropenem, montmorillonite, nadroparin, octreotide, omeprazole, phloroglucinol, silybum marianum, sulperazon, terlipressin, thymopentin, unspecified herbal and traditional medicine (gu chang zhi xie capsule, traditional chinese medicine), vitamins, and zolpidem. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at right lobe of liver, multiple sites of liver, and retroperitoneum lymphadenopathy. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 19 Apr 2016 (Day 544), the subject experienced cholestatic jaundice (Grade 3). On 30 Apr 2016 (Day 555), the study drug was withdrawn due to cholestatic jaundice and the subject received the last dose of the study drug on 29 Apr 2016 (Day 554). On 03 May 2016 (Day 558), the subject was hospitalized for cholestatic jaundice. Laboratory tests showed increased conjugated bilirubin, AST 1961 U/L (NR: 15 – 40), ALP 922 U/L (NR: 45 – 125), ALT 1642 U/L (NR: 9 – 50), total bilirubin 244.8 umol/L (NR: 3.4 – 20.4), albumin 32 g/L (NR: 40 – 55), GGT 578 U/L (NR: 11 – 50), and ammonia 42 umol/L (NR: 9 – 30). The subject was treated with alprostadil, glycyrrhiza glabra, sulperazon, anisodamine, diazepam, iohexol, octreotide, terlipressin, fentanyl, gabexate, omeprazole, montmorillonite, human albumin, octreotide, meropenem, nadroparin, lactulose, thymopentin, hyoscine, alanyl glutamine, phloroglucinol, and vitamins. On 03 May 2016 (Day 558), abdominal ultrasound showed lymph node enlargement of the portal area, liver cirrhosis, and expansion of bile duct of liver both inside and outside. On the same day (Day 558), tumor response assessment showed disease progression. The subject underwent endoscopic retrograde biliary drainage to relieve the obstruction. On 04 May 2016 (Day 559), the subject was withdrawn from study due to disease progression. The subject did not recover from cholestatic jaundice. The Investigator considered the cholestatic jaundice serious and possibly related to the study drug, and related to disease progression.

On 02 Aug 2016 (Day 649, 95 days after the last dose), the subject died due to unknown reason.

Subject Number	24171003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01549-CLI-CN
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Neutrophil count decreased

A 60-year-old Chinese female was diagnosed with hepatocellular carcinoma on 14 Dec 2011. Significant medical history included cholecystectomy, hepatitis B, hypertension, and myomectomy. Previous anticancer therapies included hepatectomy, radiofrequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included dexamethasone, enalapril, entecavir, filgrastim, granulocyte colony stimulating factor, iodine in alcohol, lidocaine, and nifedipine. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left liver lobe; masses at left lower and right upper lobes of lung. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 30 Jun 2014 (Day 54), the subject experienced decreased neutrophil count (Grade 2) and decreased white blood cell count (Grade 2). Laboratory tests showed absolute neutrophil count 1.1 x10^9/L (NR: 1.7 – 7.9) and WBC 2 x10^9/L (NR: 3.7 – 11). The subject was treated with filgrastim. On 28 Jul 2014 (Day 82), the severity of decreased neutrophil count worsened to Grade 4 with absolute neutrophil count 1.4 x10^9/L. On 31 Jul 2014 (Day 85), the severity of decreased white blood cell worsened to Grade 3 with WBC 1.6 x10^9/L and absolute neutrophil count 0.4 x10^9/L. The subject was treated with granulocyte colony stimulating factor. On 01 Aug 2014 (Day 86), the subject recovered from decreased neutrophil count and decreased white blood cell with absolute neutrophil count 8.2 x10^9/L and WBC 9.7 x10^9/L respectively. On 02 Aug 2014 (Day 87), the study drug was reduced to 8 mg/day due to decreased neutrophil count. The Investigator considered decreased neutrophil count serious (life threatening) and probably related to the study drug; decreased white blood cell count nonserious and probably related to the study drug.

On 22 Sep 2015 (Day 503), tumor response assessment showed disease progression. On 25 Sep 2015 (Day 506), 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 506).

Subject Number	24201004
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-006890
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Bone marrow failure
AE(s) Leading to Discontinuation	Bone marrow failure

A 65-year-old Chinese male was diagnosed with hepatocellular carcinoma on 03 Jun 2014. Significant medical history included cholecystitis, chronic gastritis, coronary artery arteriosclerosis, gastric varices, hepatitis B, hepatic cirrhosis, hepatic cyst, pneumonitis, and old benign left lung upper lobe lesions. Previous anticancer therapies included regional chemotherapy, high frequency ablation, panax ginseng, and unspecified herbal and traditional medicine (TCM, ganfule, and unknown ingredient). Prior and concomitant medications included amino acids, brucea javanica, dexamethasone, filgrastim, glutathione, granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, human albumin, ibuprofen, levoglutamide, mannatide, megestrol, oprelvekin, promethazine, recombinant human thrombopoietin, ribonucleic acid, thymopentin, and unspecified herbal and traditional medicine (TCM, unknown components, kang ai, and huang lian su). 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 05 Sep 2014 (Day 1), treatment with study drug was initiated.

On 29 Sep 2014 (Day 25), the subject experienced decreased platelet count (Grade 2). See table below for platelet count. Treatment included recombinant human interleukin 11 and filgrastim. The subject did not recover from decreased platelet count. The Investigator considered this event nonserious and possibly related to the study drug.

On 24 Dec 2014 (Day 111), the subject experienced bone marrow failure (myelosuppression low platelet count; Grade 3) and the study drug was interrupted on 27 Dec 2014 (Day 114). Treatment included recombinant human interleukin 11, ribonucleic acid, TCM (javanica oil emulsion injection), compound amino acids, recombinant human thrombopoietin, dexamethasone, and granulocyte macrophage colony stimulating factor. On 30 Dec 2014 (Day 117), the subject's condition improved and the severity of bone marrow failure improved to Grade 2. On 02 Jan 2015 (Day 120), the study drug was resumed at the same dose. The Investigator considered bone marrow failure nonserious and probably related to the study drug.

On 15 Feb 2015 (Day 164), the subject's bone marrow failure worsened to Grade 3. See table below. The subject was treated with recombinant human thrombopoietin and granulocyte macrophage colony stimulating factor. On 18 Feb 2015 (Day 167), the study drug was interrupted due to this event. On 20 Feb 2015 (Day 169), the severity of bone marrow failure decreased to Grade 2. On 21 Feb 2015 (Day 170), the study drug was resumed at a reduced dose of 4 mg/day due to bone marrow failure. The subject did not recover from bone marrow failure.

The Investigator considered bone marrow failure nonserious and possibly related to the study drug.

On 14 Apr 2015 (Day 222), the severity of bone marrow failure increased to Grade 3 and the subject was treated with recombinant human thrombopoietin. On 17 Apr 2015 (Day 225), the study drug was interrupted due to this event. On 25 Apr 2015 (Day 233), the severity of bone marrow failure improved to Grade 2. On 27 Apr 2015 (Day 235), the study drug was resumed at a reduced frequency of 4 mg every other day due to bone marrow failure. The subject did not recover from bone marrow failure. The Investigator considered bone marrow failure nonserious and possibly related to the study drug.

On 12 May 2015 (Day 250), the subject experienced worsening of bone marrow failure (Grade 4). On 15 May 2015 (Day 253), the study drug was interrupted due to this event. On 16 May 2015 (Day 254), the subject was hospitalized for bone marrow failure. The subject was treated with recombinant human thrombopoietin, platelet transfusion, and fresh frozen plasma transfusion. On 18 May 2015 (Day 256), the severity of bone marrow failure decreased to Grade 3. On 19 May 2015 (Day 257), the severity of bone marrow failure increased to Grade 4. The subjected was treated with clotting factor transfusion, dexamethasone, granulocyte macrophage colony stimulating factor, platelet transfusion, and fresh frozen plasma transfusion. On 21 May 2015 (Day 259), the severity of bone marrow failure decreased to Grade 2 and the subject was discharged from the hospital. The subject did not recover from bone marrow failure. The Investigator considered bone marrow failure serious and possibly related to study drug.

On 25 May 2015 (Day 263), the subject was withdrawn from the study due to bone marrow failure and received the last dose of the study drug on 14 May 2015 (Day 252). On 27 May 2015 (Day 265), the severity of bone marrow failure increased to Grade 4 and the subject was treated with unspecified herbal and traditional medicine (TCM, unknown ingredients). Due to the persistence of bone marrow failure, the subject was hospitalized on 07 Jun 2015 (Day 276) and was treated with platelet transfusion. No further information could be obtained. The subject did not recover from bone marrow failure. The Investigator considered bone marrow failure serious and possibly related to the study drug.

Table RBC, WBC, Absolute Neutrophils Count, Absolute Lymphocyte Count, and Platelet Count

Laboratory Test Date (Day)	RBC NR: 4 – 5.6 x10^12/L	WBC NR: 3.7 – 11 x10^9/L	Absolute Neutrophils Count NR:1.7 – 7.9 x10^9/L	Absolute Lymphocyte Count NR: 0.9 – 3.6 x10^9/L	Platelet Count NR:125 – 375 x10^9/L
02 Sep 2014 (Day –3) (Screening)	4.26	4.9	3	1.3	93
29 Sep 2014 (Day 25)	4.61	3.7	1.7	1.3	74
28 Oct 2014 (Day 54)	4.7	2.9	1.4	1	82
25 Nov 2014 (Day 82)	4.7	4.1	1.5	1.6	63
24 Dec 2014 (Day 111)	3.91	3.3	1.3	1.1	34
20 Jan 2015 (Day 138)	4.3	3.2	1.6	1.2	66
15 Feb 2015 (Day 164)	3.93	3	1.4	1	48
17 Mar 2015 (Day 194)	3.98	3.3	1.7	0.8	72
14 Apr 2015 (Day 222)	4.16	3.1	1.7	0.9	39
21 Apr 2015 (Day 229)	3.87	3.3	2	0.8	48
12 May 2015 (Day 250)	3.87	3.2	1.8	0.9	21
19 May 2015 (Day 257)	3.13	3.8	2.4	1.1	16
27 May 2015 (Day 265)	3.98	3.1	1.8	1.1	20

Subject Number	24181004
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-001185
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Infection (2x)

A 32-year-old Chinese female was diagnosed with hepatocellular carcinoma on 14 Oct 2014. Significant medical history included cesarean section, chronic hepatitis B, diabetes mellitus, nephrolithiasis, and splenomegaly. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included adefovir, amino acids with fats and glucose, amoxicillin, anisodamine, bacillus subtilis, berberine, codeine, drotaverine, furosemide, general nutrients, glutathione, glycyrrhiza glabra, heparin, imipenem, indometacin, irbesartan, lansoprazole, lidocaine, lornoxicam, meropenem, montmorillonite, moxifloxacin, nifedipine, ornidazole, osmotan, pancreatin, pantoprazole, paracetamol, piperacillin/tazobactam, polysaccharide-iron complex, potassium, sodium bicarbonate, spironolactone, teicoplanin, telmisartan, teprenone, tilactase, unspecified herbal and traditional medicine (shenmai zhusheye, fupu ganmao keli, xiaopiling keli, kang fu xin), valsartan, vinpocetine, and water for injection. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes, multiple sites of liver and lung, and lymphadenopathies at right inguinal, right iliac, paravertebral, retroperitoneal, and porta-hepatis lymph nodes. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

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

On 21 Oct 2014 (Day –8), the subject was hospitalized for infection (body site unknown) (Grade 3) with temperature of 38.7 ºC and palpitations with heart rate 123 bpm. Laboratory tests showed WBC 9.7 x10^9/L (NR: 3.7 – 11) and absolute neutrophils count 7.6 x10^9/L (NR: 1.7 – 7.9). The subject was treated with moxifloxacin, imipenem, meropenem, piperacillin/tazobactam, and unspecified herbal and traditional medicine (fupu ganmao keli). On 27 Oct 2014 (Day –2), the subject recovered from the infection. The Investigator considered infection serious and not related to the study drug.

On 30 Oct 2014 (Day 2), the subject was hospitalized for another episode of infection (Grade 3) (body site unknown) with temperature 39.5 ºC, dry cough, fatigue, palpitations, and chest tightness. On 31 Oct 2014 (Day 3), laboratory tests showed WBC 14.5 x10^9/L (NR: 3.5 – 9.5), absolute neutrophils 10.3 x10^9/L (NR: 1.8 – 6.3), and CRP 218.8 mg/L (NR: 0 – 5). On 02 Nov 2014 (Day 5), the study drug was interrupted due to infection. On 03 Nov 2014 (Day 6), ultrasonography of abdomen showed diffuse space-occupation of liver; coarse and mildly thickened gallbladder wall was suspected. On 04 Nov 2014 (Day 7), chest x-ray showed mildly increased markings on both lungs. The possibility of infection was suspected and infectious lesion was still not clear. Echocardiography showed tachycardia. The subject was treated with meropenem, imipenem, paracetamol, indometacin, ornidazole, osmotan, potassium, and teicoplanin. On 07 Nov 2014 (Day 10), the study drug was resumed at same dose. On

14 Nov 2014 (Day 17), the subject recovered from infection. The Investigator considered infection serious and not related to the study drug.

On 28 Sep 2015 (Day 335), tumor response assessment showed disease progression. On 30 Sep 2015 (Day 337), the subject was withdrawn from study due to disease progression. The subject continued to take the study drug despite the Investigator's decision to stop the study drug. The subject took the last dose of study drug on 02 Oct 2015 (Day 339).

On 26 Jan 2016 (Day 455, 116 days after the last dose), the subject died due to disease progression.

Subject Number	24201006
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2016-013359
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Appendiceal abscess, Postoperative abscess

A 43-year-old Chinese male was diagnosed with hepatocellular carcinoma on 18 Sep 2014. Significant medical history included hepatitis B. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included atropine, bicart (calcium chloride/glucose/magnesium chloride/potassium chloride/sodium chloride), brucea javanica, bucinnazine, cefotiam, ceftriaxone, diazepam, fats, furosemide, glycerol, hemocoagulase, human albumin, insulin, lactulose, lipids, metoclopramide, montmorillonite, morphine, omeprazole, ornidazole, palonosetron, pethidine, piperacillin w/sulbactam, potassium, proliv, sodium chloride, sulperazon, unspecified herbal and traditional medicine (huang lian su, bozhi glycopeptide, xue bi jing zhu she ye), urea, and veramid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe; bilateral lung masses and mass approaching the atrium inferior vena cava. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 27 Sep 2014 (Day 1), treatment with study drug was initiated.

On 04 Jan 2016 (Day 465), the subject experienced abdominal pain and was hospitalized for appendiceal abscess (Grade 3). The CT scan and ultrasound of abdomen showed no abnormalities. The subject was treated with bucinnazine, lipids, metoclopramide, proliv, morphine, veramid, glycerol, sulperazon, ornidazole, piperacillin w/sulbactam, bicart, cefotiam, and omeprazole. On 12 Jan 2016 (Day 473), the study drug was interrupted due to appendiceal abscess. On 13 Jan 2016 (Day 474), repeat CT scan of abdomen showed appendiceal thickening, wall thickening, and density of the surrounding liquid, suggestive of appendicitis. On 15 Jan 2016 (Day 476), the subject underwent laparotomy with ileocecal resection and jejunum-ascending colon anastomosis. Gangrenous appendix roots fecal impaction causing adjacent cecal wall penetrating ulcer were noted and the diagnosis of appendiceal abscess was confirmed. On 31 Jan 2016 (Day 492), the subject recovered from appendiceal abscess and was discharged from the hospital. On 01 Feb 2016 (Day 493), the study drug was resumed at the same dose. The Investigator considered appendiceal abscess serious and not related to the study drug.

On 07 Feb 2016 (Day 499), the subject experienced postoperative abscess (Grade 3) with right lower quadrant abdominal pain and pus at original surgical drainage tube mouth. On 12 Feb 2016 (Day 504), the subject was hospitalized for postoperative abscess and the study drug was interrupted due to the event. No laboratory tests were provided. The subject was treated with ornidazole, ceftriaxone, lactulose, and bicart. On 17 Feb 2016 (Day 509), the event improved to Grade 1 and the subject was discharged from hospital. The subject did not recover from postoperative abscess. The Investigator considered postoperative abscess serious and possibly related to the study drug.

On 24 Feb 2016 (Day 516), tumor response assessment showed disease progression. The subject received the last dose of the study drug on 11 Feb 2016 (Day 503). On 03 Mar 2016 (Day 524), the subject was withdrawn from the study due to disease progression.

On 28 May 2016 (Day 610, 107 days after the last dose), the subject died due to disease progression.

Subject Number	24211001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-006203
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Proteinuria

A 50-year-old Chinese male was diagnosed with hepatocellular carcinoma on 30 Dec 2011. Significant medical history included abdominal pain, cholecystitis, chronic hepatitis B, hepatic cirrhosis, and left renal cyst. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included calcium dobesilate, entecavir, morphine, sodium chloride, tramadol, unspecified herbal and traditional medicine (shenfukang and bailing), and valsartan. 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 6.

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

On 04 Feb 2015 (Day 141), the subject experienced proteinuria (Grade 2) with urine protein dipstick 1+. See table below. On 21 Apr 2015 (Day 217), the subject was hospitalized for persistent proteinuria and the study drug was interrupted due to proteinuria. The subject was treated with calcium dobesilate and unspecified herbal and traditional medicine (shenfukang and bailing). On 05 May 2015 (Day 231), the study drug was resumed at same dose. On 13 May 2015 (Day 239), the severity of proteinuria improved to Grade 1. The event of proteinuria was ongoing. The Investigator considered proteinuria serious and probably related to the study drug.

On 13 May 2015 (Day 239), the subject experienced hypertension (Grade 2) with blood pressure of 131/92 mmHg and was treated with valsartan. On 26 May 2015 (Day 252), proteinuria worsened to Grade 2. On 10 Jun 2015 (Day 267), the severity of proteinuria improved to Grade 1. On the same day (Day 267), the study drug was interrupted due to proteinuria and hypertension. On 30 Jun 2015 (Day 287), the subject recovered from hypertension. On 16 Jul 2015 (Day 303), the study drug was resumed at a reduced dose of 4 mg/day due to these events. The subject did not recover from proteinuria. The Investigator considered proteinuria and hypertension nonserious and probably related to the study drug.

On 11 May 2016 (Day 603), the subject experienced increased urine bilirubin (Grade 1) with urine bilirubin 2+. On the same day (Day 603), the study drug was interrupted due to increased urine bilirubin and ongoing proteinuria. On 18 May 2016 (Day 610), the subject experienced increased blood bilirubin (Grade 1) with total bilirubin 28.6 umol/L (NR: 0 – 18.8). On 25 May 2016 (Day 617), the subject experienced increased aspartate aminotransferase (Grade 4) with AST 1395 U/L (NR: 10 – 43) which started on 27 Apr 2016 (Day 589) as Grade 3. On 15 Jun 2016 (Day 638), the subject experienced increased alanine aminotransferase (Grade 2) with ALT 185 U/L (NR: 10 – 40) which started on 27 Apr 2016 (Day 589) as Grade 3. The study drug remained interrupted due to these events. On 02 Jul 2016 (Day 655), the study drug

was resumed at a reduced frequency of 4 mg every other day due to these events. The subject did not recover from increased urine bilirubin, increased blood bilirubin, increased aspartate aminotransferase, and increased alanine aminotransferase. It was unknown if the subject recovered from proteinuria. The Investigator considered proteinuria nonserious and probably related to the study drug; increased urine bilirubin, increased blood bilirubin, increased aspartate aminotransferase, and increased alanine aminotransferase nonserious and not related to the study drug.

On 20 Jul 2016 (Day 673), tumor response assessment showed disease progression. On 12 Aug 2016 (Day 696), the subject was withdrawn from the study due to disease progression and received the last dose on 17 Aug 2016 (Day 701) as the subject refused to stop the study drug.

Table 24h Urine Protein and Urine Protein Dipstick

Laboratory Test Date (Day)	24h Urine Protein (g/24hr)	Urine Protein Dipstick
04 Feb 2015 (Day 141)	Not Done	1+
16 Apr 2015 (Day 212)	3.1524	Not Done
13 May 2015 (Day 239)	Not Done	2+
14 May 2015 (Day 240)	0.9487	Not Done
27 May 2015 (Day 253)	2.2656	Not Done
10 Jun 2015 (Day 267)	0.6188	3+

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Subject Number	24221003
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2015-008155
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Blood bilirubin increased

A 46-year-old Chinese male was diagnosed with hepatocellular carcinoma on 01 May 2014. Significant medical history included hepatitis B. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included celecoxib, glutathione, ofloxacin, phospholipids, sulperazon, telbivudine, tramadol, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right liver lobes and multiple tumor lesions in liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

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

On 17 Jun 2015 (Day 308), the subject experienced increased blood bilirubin (Grade 4) with total bilirubin 242.3 umol/L (NR: 0 – 18.8) and on the same day (Day 308), the study drug was interrupted due to this event. On 18 Jun 2015 (Day 309), the subject experienced hepatitis B infection (active; Grade 2) with increased HBV-DNA polymerase levels of 1.5 x10^6 IU/ml. On 25 Jun 2015 (Day 316), the subject was hospitalized for increased blood bilirubin and was treated with ursodeoxycholic acid and phospholipids. On 10 Jul 2015 (Day 331), the subject was discharged from the hospital with recovering bilirubin levels. On 21 Jul 2015 (Day 342), the subject recovered from hepatitis B infection. On 03 Aug 2015 (Day 355), the severity of increased blood bilirubin improved to Grade 1 with the total bilirubin 30 umol/L (NR: 5 – 20.5). On 07 Aug 2015 (Day 359), the study drug was resumed at a reduced dose of 8 mg/day due to increased blood bilirubin. On 12 Aug 2015 (Day 364), the subject recovered from increased blood bilirubin with total bilirubin 18.1 umol/L (NR: 0 – 18.8). The Investigator considered increased blood bilirubin serious and possibly related to the study drug; hepatitis B infection nonserious and not related to the study drug.

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

Subject Number	24221005
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	EC-2014-000825
Assigned Treatment	Lenvatinib 12 mg/day
Non-Fatal SAE(s)	Periodontitis

A 57-year-old Chinese male was diagnosed with hepatocellular carcinoma on 30 Sep 2011. Significant medical history included alcoholic cirrhosis, chronic gastritis, and hepatitis B. Previous anticancer therapies included transcatheter arterial chemoembolization (5x) and microwave therapy. Prior and concomitant medications included esomeprazole, mosapride, pantoprazole, and piperacillin/tazobactam. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right and left liver lobes; lymphadenopathy at multiple sites of liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

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

On 18 Sep 2014 (Day 8), the subject experienced periodontitis (Grade 1). On 02 Oct 2014 (Day 22), the severity of periodontitis worsened to Grade 2 and the subject was hospitalized. The subject was treated with piperacillin/tazobactam. On 06 Oct 2014 (Day 26), the study drug was interrupted due to periodontitis. On 13 Oct 2014 (Day 33), the subject recovered from periodontitis. On 17 Oct 2014 (Day 37), the study drug was resumed at same dose. The Investigator considered periodontitis serious and not related to the study drug.

On 07 Nov 2014 (Day 58), tumor response assessment showed disease progression. On 10 Nov 2014 (Day 61), 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 61).

On 03 Feb 2015 (Day 146, 85 days after the last dose), the subject died due to disease progression.

Subject Number	30011001
Study Name	E7080-G000-304
Eisai Manufacturer's Control Number	E7080-01402-CLI-KR
Assigned Treatment	Lenvatinib 8 mg/day
Non-Fatal SAE(s)	Ascites

A 76-year-old Asian female was diagnosed with hepatocellular carcinoma on 17 Jan 2007. Significant medical history included upper abdominal pain, hepatitis C, liver cirrhosis, and cerebrovascular disorder (bilateral cerebral small vessel disease). Previous anticancer therapies included percutaneous ethanol injection and transcatheter arterial chemoembolization. Prior and concomitant medications included acetylcarnitine, amlodipine, cebetabs, famotidine, furosemide, glucose, human albumin, lactulose, lekovit ca, raloxifene, silybum marianum, spironolactone, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right lobes of liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 6.

On 19 Jul 2013 (Day 1), treatment with study drug was initiated.

On 03 Aug 2013 (Day 16), the subject experienced hepatic encephalopathy (Grade 1). On 14 Aug 2013 (Day 27), the event worsened to Grade 2. The study drug was interrupted due to this event and the subject was treated with lactulose. On 20 Aug 2013 (Day 33), the severity of hepatic encephalopathy improved to Grade 1 and study drug was resumed at reduced dose of 4 mg/day due to hepatic encephalopathy. On 26 Aug 2014 (Day 39), the subject recovered from hepatic encephalopathy. The Investigator considered hepatic encephalopathy nonserious and possibly related to study drug.

On 05 Nov 2013 (Day 110), tumor response assessment showed disease progression. On 08 Nov 2013 (Day 113), the subject was withdrawn from the study due to disease progression and on the same day (Day 113), the subject received the last dose of study drug.

On 16 Nov 2013 (Day 121), the subject was hospitalized for ascites (Grade 3). The subject underwent paracentesis and also received treatment with intravenous albumin, glucose, furosemide, and spironolactone. On 26 Nov 2013 (Day 131), the severity of ascites improved to Grade 2. The subject did not recover from this event. The Investigator considered this event serious and not related to study drug.

On 23 Dec 2013 (Day 158, 45 days after the last dose), the subject died due to disease progression.