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| Subject Number | 14061019 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2016-021628 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Myocardial infarction |
| AE(s) Leading to Discontinuation | Myocardial infarction |

A 63-year-old white male was diagnosed with hepatocellular carcinoma on 11 Jul 2014. Significant medical history included tobacco user, alcohol use, anal fistula, arterial hypertension, hepatic cirrhosis, esophageal variceal ligation, gastritis, glaucoma, hepatitis C, hip arthroplasty, obesity, gastroesophageal reflux disease, right inguinal hernia, and inguinal hernia repair. Previous anticancer therapy included transcatheter arterial chemoembolization (2x). Prior and concomitant medications included amlodipine, carteolol, dexeryl, furosemide, latanoprost, loperamide, nadolol, omeprazole, other dermatological preparations (salicylate vaseline), panadeine co, spironolactone, and xerial. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of liver and multiple sites of liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

On 07 May 2015 (Day 1), treatment with study drug was initiated.

On 02 May 2016 (Day 362), the subject experienced proteinuria (Grade 2) with urine protein dipstick 3+. On 18 Jun 2016 (Day 409), the study drug was interrupted due to the event. On 22 Jun 2016 (Day 413), the severity of proteinuria improved to Grade 1. On 27 Jun 2016 (Day 418), the study drug was resumed at same dose. The subject did not recover from proteinuria. The Investigator considered proteinuria nonserious and probably related to study drug.

On 29 Aug 2016 (Day 481), tumor response assessment showed stable disease, which was reassessed and later confirmed as disease progression on 16 Dec 2016 (Day 590).

On 22 Oct 2016 (Day 535), the subject was admitted to the hospital in cardiorespiratory arrest and after resuscitation, the subject was in coma (Grade 3) and was diagnosed with myocardial infarction (Grade 4). On 17 Nov 2016 (Day 561), the subject recovered from coma. On 06 Dec 2016 (Day 580), the subject recovered from myocardial infarction. On 07 Dec 2016 (Day 581), the subject was withdrawn from study due to myocardial infarction and received the last dose of study drug on 22 Oct 2016 (Day 535). The Investigator considered myocardial infarction serious and not related to study drug; coma nonserious and not related to study drug.

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| Subject Number | 14061021 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-007706 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Abdominal pain, Asthenia, Hepatic encephalopathy |

A 38-year-old African American male was diagnosed with hepatocellular carcinoma in May 2014. Significant medical history included hepatitis B and pulmonary embolism. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included domperidone, enoxaparin, entecavir, hydroxyzine, lactulose, morphine, oxycodone, pantoprazole, and tenofovir. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right lobes of liver and portal vein. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 11 Jun 2015 (Day 4), the subject was hospitalized for abdominal pain (abdominal pain related to palpable hepatic mass; Grade 3) and the subject was treated with oxycodone. On the same day (Day 4), the subject experienced asthenia (Grade 2). On 17 June 2015 (Day 10), asthenia worsened to Grade 3 and on 18 Jun 2015 (Day 11), the study drug was interrupted due to asthenia. On 22 Jun 2015 (Day 15), the subject recovered from asthenia and the study drug was resumed at reduced dose of 8 mg/day due to asthenia. On 25 Jun 2015 (Day 18), the subject recovered from abdominal pain. The Investigator considered asthenia serious and probably related to study drug; abdominal pain serious and not related to study drug.

On 19 Aug 2015 (Day 73), tumor response assessment showed disease progression. On 20 Aug 2015 (Day 74), the subject was withdrawn from the study due to disease progression and received the last dose on 19 Aug 2015 (Day 73).

On 19 Aug 2015 (Day 73), the subject was hospitalized for hepatic encephalopathy (Grade 1). Laboratory tests showed total bilirubin 39 umol/L (NR: 0 – 17), AST 436 U/L (NR: 0 – 35), ALT 43 U/L (NR: 0 – 43), ALP 172 U/L (NR: 0 – 115), and CRP 208.5 mg/L (NR: 0 – 5). Treatment included lactulose. On 20 Aug 2015 (Day 74), hepatic encephalopathy worsened to Grade 2. On 31 Aug 2015 (Day 85), repeat laboratory tests showed total bilirubin 18.1 umol/L (NR: 0 – 18.8), ALP 893 U/L (NR: 43 – 115), ALT 57 U/L (NR: 10 – 40), and AST 156 U/L (NR: 10 – 43). On 01 Sep 2015 (Day 86), the subject was discharged from the hospital. The subject did not recover from this event. The Investigator considered hepatic encephalopathy serious and not related to study drug.

On 14 Oct 2015 (Day 129, 56 days after the last dose), the subject died and it was unknown if the death was due to disease progression.

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| Subject Number | 14131001 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01571-CLI-FR |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Hepatic encephalopathy, Headache, Jaundice |

A 54-year-old white male was diagnosed with hepatocellular carcinoma on 26 Nov 2013. Significant medical history included hepatic cirrhosis, decreased blood albumin, and hepatitis C. Previous anticancer therapies included hepatectomy and radioembolization (2x). Prior and concomitant medications included acetylcysteine, augmentin, cetirizine, desloratadine, furosemide, helicidine, lactulose, omeprazole, paracetamol, prednisolone, spasfon, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed intra-aortic caval, para-caval, and reno-caval lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

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

On 31 Aug 2014 (Day 11), the subject was hospitalized for hepatic encephalopathy (Grade 3). On 01 Sep 2014 (Day 12), the study drug was interrupted due to hepatic encephalopathy and the subject was treated with lactulose. On 03 Sep 2014 (Day 14), the laboratory tests showed albumin 32 g/L (NR: 35 – 55), ALP 262 U/L (NR: 43 – 115), ALT 42 U/L (NR: 10 – 40), AST 128 U/L (NR: 10 – 43), and total bilirubin 17.6 umol/L (NR: 0 – 18.8). On the same day (Day 14), the study drug dose was resumed at a reduced frequency of 8 mg every other day due to hepatic encephalopathy and the subject was discharged from the hospital. On 17 Sep 2014 (Day 28), the subject recovered from hepatic encephalopathy. The Investigator considered hepatic encephalopathy serious and probably related to the study drug.

On 28 Jun 2015 (Day 312), the subject was hospitalized for headache (Grade 3) which was ongoing since 26 Apr 2015 (Day 249) as Grade 1. The study drug dose did not change. On 02 Jul 2015 (Day 316), the subject was hospitalized for jaundice (Grade 2). The subject experienced increased blood bilirubin (Grade 3), fatigue (Grade 2), and asthenia (Grade 2). Laboratory results showed AST 654 U/L (NR: 10 – 45), ALT 195 U/L (NR: 5 – 50), ALP 305 U/L (NR: 40 – 130), total bilirubin 98 umol/L (NR: 3 – 18), conjugated bilirubin 61 mmol/L (NR: 0 – 5), and sodium 129 mmol/L (NR: 135 – 145). The subject was treated with tramadol and prednisolone. On the same day (Day 316), the subject recovered from headache. On 03 Jul 2015 (Day 317), the study drug was interrupted due to jaundice and the subject was treated with prednisolone. On 09 Jul 2015 (Day 323), the subject experienced decreased blood albumin (Grade 3) which was ongoing since 17 Sep 2014 (Day 28) as Grade 2 with albumin 19 g/L. The subject did not recover from jaundice, fatigue, asthenia, increased blood bilirubin, and decreased blood albumin. The Investigator considered headache serious and not related to study drug; jaundice serious and not related to the study drug but related to disease progression; increased blood bilirubin and decreased blood albumin nonserious and not related to the study drug but related to disease progression; asthenia and fatigue nonserious and not related to the study drug.

On 02 Jul 2015 (Day 316), tumor response assessment showed disease progression however, scans on 15 Oct 2014 (Day 56) were initially assessed as stable disease which on 10 Nov 2015 (Day 447), were reassessed as progressive disease. On 09 Jul 2015 (Day 323), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on 02 Jul 2015 (Day 316).

On 15 Aug 2015 (Day 360, 44 days after the last dose), the subject died due to disease progression. Autopsy was not performed.

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| Subject Number | 14141002 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-002969 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Pathological fracture |

A 74-year-old white male was diagnosed with hepatocellular carcinoma on 14 Nov 2014. Significant medical history included decreased appetite, diabetes mellitus, palmoplantar keratoderma, hypertension, hypercholesterolemia, myocardial ischemia, ankle fracture, meniscus operation, back pain, and decreased weight. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amoxicillin, atorvastatin, bisoprolol, carbohydrates with fats and minerals, coveram, enoxaparin, fentanyl, glimepiride, homeopatics (stodal), lekovit ca, levothyroxine, macrogol, metformin, morphine, ofloxacin, paracetamol, paraffin liquid, ramipril, sitagliptin, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left liver lobe, left branch portal invasion of liver, and thoracic vertebral mass. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 02 Jan 2015 (Day 11), the subject experienced back pain (Grade 2) and was treated with tramadol, fentanyl, paracetamol, and morphine. On 08 Jan 2015 (Day 17), the subject was hospitalized with pathological fracture (osteolytic vertebra fracture; Grade 3). The CT scan of spine showed broken fourth thoracic vertebra. The subject was treated with splint application (chest corset), fentanyl, paracetamol, and morphine. On 15 Jan 2015 (Day 24), severity of pathological fracture improved to Grade 2. On 11 Mar 2015 (Day 79), the subject recovered from pathological fracture. The subject did not recover from back pain. The Investigator considered pathological fracture serious and not related to the study drug; back pain nonserious and not related to the study drug.

On 04 Aug 2015 (Day 225), tumor response assessment showed disease progression. On 11 Aug 2015 (Day 232), the subject was withdrawn from study due to disease progression and received the last dose of study drug on 10 Aug 2015 (Day 231).

On 21 Jan 2016 (Day 395, 164 days after the last dose), the subject died due to disease progression.

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| Subject Number | 15051008 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2014-002321 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Seizure |

A 71-year-old white male was diagnosed with hepatocellular carcinoma on 20 Jul 2011. Significant medical history included hypertension, hepatitis C, hepatic cirrhosis, squamous cell carcinoma of skin, and skin neoplasm excision. Previous anticancer therapies included hepatectomy (2x) and high frequency ablation (2x). Prior and concomitant medications included furosemide, levothyroxine, omeprazole, phenobarbital, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe and right pleural masses. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 06 Dec 2014 (Day 205), the subject was hospitalized for seizure (Grade 4) and study drug was interrupted due to the event. Computerized tomography of brain showed brain metastases. Treatment included phenobarbital. On 13 Dec 2014 (Day 212), the subject recovered from this event and was discharged from the hospital. The Investigator considered seizure serious and not related to the study drug but related to disease progression.

On 23 Dec 2014 (Day 222), the subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of study drug on 05 Dec 2014 (Day 204).

On 17 Jan 2015 (Day 247, 43 days after the last dose), the subject died due to disease progression.

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| Subject Number | 16011005 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2014-000305 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Hepatic failure |
| AE(s) Leading to Discontinuation | Hepatic failure |

A 49-year-old white male was diagnosed with hepatocellular carcinoma on 10 Mar 2014. Significant medical history included esophageal varices, hepatitis C, hypertension, hepatic cirrhosis, and portal hypertension. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included electrolyte solutions, glucose, heparin, levothyroxine, loperamide, mometasone, propranolol, and sodium chloride. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe and porta-hepatitis lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 23 Jun 2014 (Day 57), the subject experienced hypothyroidism (Grade 2). The subject was treated with levothyroxine. On 27 Jun 2014 (Day 61), the subject experienced fatigue (Grade 3) and diarrhea (Grade 2). The subject was treated with loperamide. On 30 Jun 2014 (Day 64), the subject experienced vomiting (Grade 1). On 04 Jul 2014 (Day 68), the study drug was interrupted due to fatigue, diarrhea, and vomiting. On 08 Jul 2014 (Day 72), the subject recovered from diarrhea, vomiting, and fatigue improved to Grade 2. On 14 Jul 2014 (Day 78), the study drug was resumed at a reduced dose of 8 mg/day due to diarrhea and fatigue. On 21 Jul 2014 (Day 85), fatigue improved to Grade 1 and the subject experienced decreased weight (Grade 2) with body weight of 97 kg (Baseline: 111 kg). The subject did not recover from hypothyroidism, fatigue, and decreased weight. The Investigator considered hypothyroidism nonserious and possibly related to the study drug; fatigue, diarrhea, vomiting, decreased weight nonserious and probably related to the study drug.

On 26 Aug 2014 (Day 121), the fatigue worsened to Grade 2 and the subject experienced dehydration (Grade 2), hyperbilirubinemia (Grade 3), decreased appetite (Grade 2), hyponatremia (Grade 3) with sodium 129 mmol/L (NR: 136 – 145), and nausea (Grade 2). The subject was treated with sodium chloride and electrolyte solutions and the study drug was interrupted due to fatigue, hyperbilirubinemia, decreased appetite, nausea, hyponatremia, hypoalbuminemia, and dehydration. On 27 Aug 2014 (Day 122), the subject experienced hepatic failure (Grade 3) and hypoalbuminemia (Grade 2). Laboratory tests were done and showed albumin 29 g/L (NR: 35 – 50), AST 94 U/L (NR: 5 – 34), ALT 56 U/L (NR: 0 – 55), lipase 84 U/L (NR: 8 – 78), total bilirubin 84.816 umol/L (NR: 3.42 – 20.52), and creatinine 108.732 umol/L (NR: 61.88 – 114.92). On 01 Sep 2014 (Day 127), repeat laboratory tests showed albumin 24 g/L, AST 107 U/L, ALT 61 U/L, ALP 113 U/L (NR: 40 – 150), sodium 128 mmol/L, platelet count 98 x10^9/L (NR: 150 – 410), and total bilirubin 185.364 umol/L. On 15 Sep 2014 (Day 141), the subject recovered from hyponatremia with

sodium 134 mmol/L (NR: 133 – 145). The subject did not recover from hepatic failure, fatigue, dehydration, hyperbilirubinemia, hypoalbuminemia, decreased appetite, and nausea. The Investigator considered hepatic failure serious (important medical event) and probably related to the study drug; dehydration, hyponatremia, and hypoalbuminemia nonserious and possibly related to the study drug; fatigue, hyperbilirubinemia, decreased appetite, and nausea nonserious and probably related to the study drug.

On 24 Oct 2014 (Day 180), the subject was withdrawn from the study due to hepatic failure and received the last dose of the study drug on 25 Aug 2014 (Day 120).

On 07 Nov 2014 (Day 194, 74 days after the last dose), the subject died due to unknown cause.

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| Subject Number | 16011008 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-009129 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Tuberculosis |

A 64-year-old white male was diagnosed with hepatocellular carcinoma on 28 Dec 2009. Significant medical history included asthma, chronic hepatitis B, chronic hepatitis C, diabetes mellitus, hypertension, hepatic cirrhosis, and myocardial infarction. Previous anticancer therapies included high frequency ablation (2x) and transcatheter arterial chemoembolization (2x). Prior and concomitant medications included acetylsalicylic acid, captopril, cefuroxime, ciclesonide, clindamycin, enalapril, entecavir, hyoscine, human insulin, ipratropium, megestrol, metronidazole, salmeterol, seretide, and telmisartan. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

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

On 31 Mar 2015 (Day 281), the subject experienced decreased weight (Grade 1) with body weight of 61.5 kg (Baseline: 68 kg). On 30 Apr 2015 (Day 311), the event worsened to Grade 2 with body weight of 59 kg. Treatment was not provided. On 26 May 2015 (Day 337), the CT scan of chest showed thick walled cavity in the left lung which was suspected for tuberculosis (Grade 1). The study drug was reduced to a dose of 8 mg/day due to decreased weight and suspected tuberculosis. On 16 Jul 2015 (Day 388), the study drug was interrupted due to suspected tuberculosis. Laboratory tests showed differential neutrophils 65.7% (NR: not provided), differential lymphocytes 22% (NR: not provided), and WBC 5.55 x10^9/L (NR: not provided). On 17 Jul 2015 (Day 389), the subject was hospitalized to undergo tuberculosis tests and bronchofiberoscopy showed normal vocal cords, trachea, and carina was clear; fungal test was negative. On 21 Jul 2015 (Day 393), the fungal test result was negative for Aspergillus. On 23 Jul 2015 (Day 395), repeat CT scan of chest showed fibrous and atrophy lesions in bilateral lungs, thick-walled cavity in the left lung (slightly larger than before), and inflammatory infiltrations were nonspecific. On 24 Jul 2015 (Day 396), polymerase chain reaction test was negative for tuberculosis. Treatment was not provided. On 30 Jul 2015 (Day 402), the subject was discharged from the hospital as the diagnosis of tuberculosis was not confirmed by the tests and the study drug was resumed at the same dose. On 09 Aug 2016 (Day 778), the subject recovered from decreased weight. The Investigator considered tuberculosis serious and not related to study drug; decreased weight nonserious and possibly related to study drug.

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

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| Subject Number | 16021010 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2016-021818 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Intervertebral disc protrusion |

A 56-year-old white female was diagnosed with hepatocellular carcinoma on 16 Sep 2014. Significant medical history included large intestinal polypectomy, hepatic cirrhosis, and myomectomy. Previous anticancer therapy included high frequency ablation. Prior and concomitant medications included aspartic acid, augmentin, ciprofloxacin, dynamag, fluconazole, ketoprofen, moduretic, ondansetron, potassium, ramipril, rifaximin, tizanidine, tramadol, and vaccinium macrocarpon. 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 5.

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

On 02 Sep 2016 (Day 625), the subject was hospitalized for lumbar pain and was diagnosed with intervertebral disc protrusion (L3 – L4; Grade 3). The MRI of spine showed lumbar discopathy: posterior lateral hernia of L3 – L4 disc. Treatment included tizanidine and tramadol. The subject was recovering from intervertebral disc protrusion and was discharged from the hospital. The Investigator considered intervertebral disc protrusion serious and not related to study drug.

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

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| Subject Number | 17021003 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-005803 |
| Assigned Treatment | Lenvatinib 8 mg/day |
| Non-Fatal SAE(s) | Decreased appetite, Weight decreased, General physical health deterioration |

A 63-year-old white male was diagnosed with hepatocellular carcinoma on 10 Jun 2014. Significant medical history included abdominal pain, alcohol abuse, allergic to typhoid vaccine, decreased appetite, cough, ear discomfort, prostatomegaly, lethargy, rash, musculoskeletal discomfort (right shoulder), and decreased weight. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amoxicillin, contact laxatives, dihydrocodeine, docusate, levothyroxine, megestrol, paracetamol, senna alexandrina, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, multiple lung metastases, left pleural effusion, and right hilar, right paratracheal, and portacaval lymphadenopathies. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

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

On 10 Feb 2015 (Day 131), the subject experienced decreased appetite (Grade 2), lethargy (Grade 2), and decreased weight (Grade 3) with body weight of 43.7 kg (Baseline: 57.9 kg). The study drug was interrupted due to these events. The subject did not recover from decreased appetite, decreased weight, and lethargy. The Investigator considered decreased appetite, decreased weight, and lethargy nonserious and possibly related to the study drug.

On 03 Mar 2015 (Day 152), the subject was withdrawn from the study due to clinical disease progression and received the last dose of the study drug on 09 Feb 2015 (Day 130).

On 10 Mar 2015 (Day 159), the subject was hospitalized for general physical health deterioration (Grade 3), worsening of decreased appetite (Grade 3), and decreased weight (Grade 3). Treatment was not reported since the subject was admitted in another hospital (source was not obtainable). The subject did not recover from decreased appetite, decreased weight, and general physical health deterioration. The Investigator considered decreased appetite, decreased weight, and general physical health deterioration serious and not related to the study drug but related to disease progression.

On 02 Apr 2015 (Day 182, 52 days after the last dose), the subject died due to clinical disease progression.

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| Subject Number | 17021004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2014-001940 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Hypoglycaemia, Pulmonary embolism |

A 72-year-old white male was diagnosed with hepatocellular carcinoma on 17 May 2012. Significant medical history included bilateral Dupuytren's contracture, musculoskeletal discomfort (left hand), hemochromatosis, hiatus hernia, hypertension, atrial fibrillation, gastric ulcer, and type 1 diabetes mellitus. Previous anticancer therapies included transcatheter arterial chemoembolization (9x). Prior and concomitant medications included dalteparin, enalapril, flucloxacillin, glucose, human insulin, lansoprazole, paracetamol, and simvastatin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right portal vein and multiple lesions at segment 5, 6, and 7 of liver. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 22 Nov 2014 (Day 3), the subject experienced hypoglycemia (Grade 4) and nausea (Grade 1) and noted that the subject had a loss of appetite for a few days and was still maintained on human insulin. On 23 Nov 2014 (Day 4), the subject was hospitalized for hypoglycemia and the subject also experienced dyspnea (Grade 1) and pain in extremity (Grade 1). The chest x-ray showed subtle increased opacification of left lung compared to right lung. The subject was treated with glucose and the study drug was interrupted due to suspected pulmonary embolism. On the same day (Day 4), the subject recovered from nausea and hypoglycemia. On 24 Nov 2014 (Day 5), the subject remained hospitalized for pulmonary embolism (Grade 3) which was confirmed by pulmonary angiogram which showed small volume pulmonary embolism in the lingular segment, bibasal atelectasis, and consolidation. Laboratory tests showed WBC 17.8 x10^9/L (NR: 4 – 11), absolute neutrophils 14.8 x10^9/L (NR: 2 – 7.5), and blood cultures were negative for infection. The subject was treated with dalteparin. On 03 Dec 2014 (Day 14), the subject recovered from pulmonary embolism and the study drug was resumed at a reduced dose of 8 mg/day due to pulmonary embolism. On 06 Jan 2015 (Day 48), the subject recovered from dyspnea and pain in extremity. The Investigator considered pulmonary embolism and hypoglycemia serious and possibly related to the study drug; dyspnea nonserious and probably related to the study drug; pain in extremity and nausea nonserious and possibly related to the study drug.

On 13 Jan 2015 (Day 55), the subject experienced proteinuria (Grade 1). Laboratory test showed 24h urine protein 0.1934 g/24hr. On 26 Jan 2015 (Day 68), the subject recovered from proteinuria. On 24 Feb 2015 (Day 97), the study drug was interrupted due to the event. The Investigator considered proteinuria nonserious and probably related to the study drug.

On 03 Mar 2015 (Day 104), tumor response assessment showed disease progression. On 10 Mar 2015 (Day 111), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on 23 Feb 2015 (Day 96).

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| Subject Number | 17021007 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-004793 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Back pain |

A 78-year-old white male was diagnosed with hepatocellular carcinoma on 13 Mar 2012. Significant medical history included aortic valve replacement, coronary artery bypass, increased blood alcohol, cholelithiasis, hiatus hernia, hypertension, hypothyroidism, abdominal pain, renal impairment, and exertional dyspnea. Previous anticancer therapies included transcatheter arterial chemoembolization (4x). Prior and concomitant medications included acetylsalicylic acid, antibiotics (unknown), antihistamines (unknown), avena sativa, budesonide w/formoterol fumarate, furosemide, lansoprazole, levothyroxine, loratadine, ondansetron, perindopril, salbutamol, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at segment 7 of the liver, segment 3 extending to segment 2 of the liver, and tip of segment 6 of the liver; and subcapsular extrahepatic deposit. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

On 25 Feb 2015 (Day 1), treatment with study drug was initiated.

On 10 Mar 2015 (Day 14), the subject was hospitalized for back pain (Grade 1) radiating to the right side of buttock to the outer aspect of the thigh and no treatment was given. The subject also experienced hyperbilirubinemia (Grade 2), increased alanine aminotransferase (Grade 1), and increased aspartate aminotransferase (Grade 1). Laboratory tests showed albumin 32 g/L (NR: 35 – 55), ALT 45 U/L (NR: 10 – 40), ALP 328 U/L (NR: 43 – 115), AST 62 U/L (NR: 10 – 43), GGT 174 U/L (NR: 10 – 49), and total bilirubin 54.4 umol/L (NR: 0 – 18.8). On the same day (Day 14), the study drug dose was reduced to 8 mg/day due to hyperbilirubinemia. On 12 Mar 2015 (Day 16), the subject recovered from hyperbilirubinemia. On 13 Mar 2015 (Day 17), MRI of spine was normal and did not show nerve root compression or cauda equina syndrome. On the same day (Day 17), the subject was discharged from the hospital. On 14 Mar 2015 (Day 18), the subject experienced burning sensation (in feet; Grade 1) and no treatment was given. On 24 Mar 2015 (Day 28), the subject recovered from increased aspartate aminotransferase and increased alanine aminotransferase. On 14 Apr 2015 (Day 49), the subject recovered from back pain and burning sensation. The Investigator considered back pain serious and not related to the study drug; hyperbilirubinemia and burning sensation nonserious and probably related to the study drug; increased aspartate aminotransferase and increased alanine aminotransferase nonserious and possibly related to the study drug.

On 28 Mar 2015 (Day 32), the subject experienced nausea (Grade 1), vomiting (Grade 1), and decreased weight (Grade 2) with body weight of 98.5 kg (Baseline: 101.6 kg). On 07 Apr 2015 (Day 42), the study drug was interrupted due to these events. On 09 Apr 2015 (Day 44), the subject recovered from nausea and vomiting. On 14 Apr 2015 (Day 49), the study drug was resumed at a reduced dose of 4 mg/day due to these events. The subject did not recover from

decreased weight. The Investigator considered nausea and vomiting nonserious and possibly related to the study drug; decreased weight nonserious and not related to the study drug.

On 26 May 2015 (Day 91), the subject experienced lethargy (Grade 2). On 02 Jun 2015 (Day 98), the study drug was interrupted due to lethargy. On 15 Jun 2015 (Day 111), severity of lethargy improved to Grade 1 and the subject did not recover from lethargy. On 16 Jun 2015 (Day 112), the study drug was resumed at a reduced frequency of 4 mg every other day due to this event. The Investigator considered lethargy nonserious and probably related to the study drug.

On 06 Oct 2015 (Day 224), tumor response assessment showed disease progression. On 13 Oct 2015 (Day 231), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 12 Oct 2015 (Day 230).

On 07 Feb 2016 (Day 348, 118 days after the last dose), the subject died due to disease progression.

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| Subject Number | 17021009 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-010704 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Pyrexia, Hepatopulmonary syndrome |

A 63-year-old white male was diagnosed with hepatocellular carcinoma in May 2014. Significant medical history included bilateral palmar erythema, increased international normalized ratio, prolonged prothrombin time, hepatitis C, abdominal discomfort (right upper quadrant), and spider nevus. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included avena sativa (supplement), cyclizine, dalteparin, omeprazole, and oxygen. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at right liver lobe. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

On 01 Jul 2015 (Day 1), treatment with study drug was initiated.

On 22 Sep 2015 (Day 84), the subject was hospitalized for pyrexia (Grade 1) with temperature of 37.9 ºC. On the same day (Day 84), the chest x-ray was normal and WBC was 5.8 x10^9/L (NR: 3.7 – 11). On 23 Sep 2015 (Day 85), the computerized tomography pulmonary angiogram was normal. The subject did not receive any treatment and the study drug dose did not change. On the same day (Day 85), the subject recovered from pyrexia and was discharged from the hospital. The Investigator considered pyrexia serious and not related to the study drug.

On 29 Sep 2015 (Day 91), the subject experienced decreased appetite (Grade 3) and lethargy (Grade 2) which was ongoing since 06 Jul 2015 (Day 6) as Grade 1. On 20 Oct 2015 (Day 112), the study drug was interrupted due to these events. On 22 Oct 2015 (Day 114), the severity of decreased appetite and lethargy improved to Grade 1. On 03 Nov 2015 (Day 126), the study drug dose was resumed at a reduced dose of 8 mg/day due to these events. On 11 Feb 2016 (Day 226), the subject recovered from decreased appetite. The subject did not recover from lethargy. The Investigator considered decreased appetite and lethargy nonserious and probably related to study drug.

On 26 Jan 2016 (Day 210), the subject was hospitalized for hepatopulmonary syndrome (Grade 2) and also experienced dyspnea (Grade 3) and hypoxia (Grade 2). The computerized tomography pulmonary angiogram showed no pulmonary embolism and oxygen saturation on lying down was 97% and on standing was 88%. Oxygen treatment was given. On 09 Feb 2016 (Day 224), the study drug was interrupted due to hepatopulmonary syndrome. Laboratory test showed elevated AST 48 U/L (NR: 10 – 43) and other liver function tests were normal. On 16 Feb 2016 (Day 231), the study drug was resumed at a reduced dose of 4 mg/day due to hepatopulmonary syndrome. On 15 Mar 2016 (Day 259), the laboratory test showed AST 39 U/L. The subject did not recover from these events. The Investigator considered hepatopulmonary syndrome serious and not related to the study drug; hypoxia and dyspnea nonserious and not related to the study drug.

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

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| Subject Number | 17031002 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-004543 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Ascites (2x), Hepatic failure |

A 72-year-old white male was diagnosed with hepatocellular carcinoma in 2010. Significant medical history included left knee arthritis, hepatic cirrhosis, depression, internal fixation of fracture (right wrist), hypertension, spinal fusion surgery (L1 – L5), and type 2 diabetes mellitus. Previous anticancer therapies included transcatheter arterial chemoembolization and high frequency ablation (2x). Prior and concomitant medications included codeine, domperidone, human albumin, hydrocortisone, paracetamol, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, right pelvic mass, and anterior mediastinal fat/right hemi-diaphragm lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 27 Nov 2014 (Day 42), the subject experienced fatigue (Grade 3). On 09 Dec 2014 (Day 54), the study drug was interrupted due to this event. On 17 Dec 2014 (Day 62), the severity of fatigue improved to Grade 1 and the study drug was resumed at a reduced dose of 8 mg/day due to fatigue. The subject did not recover from this event. The Investigator considered fatigue nonserious and probably related to the study drug.

On 06 Feb 2015 (Day 113), tumor response assessment showed disease progression. On 24 Feb 2015 (Day 131), the subject was withdrawn from the study due to disease progression. The subject received the last dose of study drug on 23 Feb 2015 (Day 130).

On 25 Feb 2015 (Day 132), the subject was hospitalized for ascites (Grade 2) and was treated with spironolactone. On 02 Mar 2015 (Day 137), the subject recovered from ascites with sequelae and was discharged from the hospital. The Investigator considered this event serious and not related to the study drug but related to disease progression.

On 06 Mar 2015 (Day 141), the subject was hospitalized for another episode of ascites (Grade 3). Laboratory tests showed albumin 31 g/L (NR: 35 – 50), ALP 159 U/L (NR: 30 – 130), and sodium 128 mmol/L (NR: 133 – 146). The subject underwent abdominal cavity drainage and was also treated with human albumin. On 12 Mar 2015 (Day 147), the subject recovered from ascites. The Investigator considered ascites serious and not related to the study drug but related to disease progression.

On 24 Mar 2015 (Day 159), the subject was hospitalized for hepatic failure (Grade 3). Abdominal x-ray showed slightly distended small bowel loops but no evidence of bowel obstruction. Laboratory tests showed albumin 32 g/L, AST 48 U/L (NR: 0 – 45), ALP 316 U/L, GGT 177 U/L (NR: 0 – 50), and total protein 59 g/L (NR: 60 – 80). The subject underwent

paracentesis. The subject did not recover from hepatic failure. The Investigator considered the event hepatic failure serious and not related to the study drug but related to disease progression.

On 16 Apr 2015 (Day 182, 52 days after the last dose), the subject died due to disease progression. Autopsy was not performed.

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| Subject Number | 17041006 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-003446 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Spinal cord compression |
| AE(s) Leading to Discontinuation | Spinal cord compression |

A 56-year-old white male was diagnosed with hepatocellular carcinoma on 01 Sep 2014. Significant medical history included alcohol use, musculoskeletal discomfort (back), constipation, and hypertension. Previous anticancer therapy included hepatectomy and radiotherapy to thoracic vertebral lesion (T6). Prior and concomitant medications included amitriptyline, amlodipine, amoxicillin, codeine, cyclizine, dexamethasone, electrolytes w/macrogol, gabapentin, hypnotics and sedatives, ibuprofen, lisinopril, morphine, other emollients and protectives (aqueous cream), paracetamol, and ranitidine. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right and left lobe of liver, widespread bone lesion, and lymphadenopathy between portal vein inferior vena cava and gallbladder. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 21 Nov 2014 (Day 10), the subject experienced hepatic failure (Grade 3). On 22 Nov 2014 (Day 11), the study drug was interrupted due to the event. On 26 Nov 2014 (Day 15), the subject experienced ascites (Grade 1). Laboratory tests showed albumin 33 g/L (NR: 35 – 55), ALP 442 U/L (NR: 43 – 115), ALT 60 U/L (NR: 10 – 40), AST 145 U/L (NR: 10 – 43), GGT 255 U/L (NR: 10 – 49), and CRP 228.2 mg/L (NR: 0 – 5). On 04 Dec 2014 (Day 23), the study drug was resumed at a reduced dose of 8 mg/day due to hepatic failure. On 10 Dec 2014 (Day 29), the subject recovered from hepatic failure and was recovering from ascites. The Investigator considered hepatic failure, ascites nonserious and possibly related to the study drug.

On 16 Dec 2014 (Day 35), the subject experienced pain in extremity (Grade 1). On 07 Jan 2015 (Day 57), the subject experienced muscular weakness (weak hip flexion; Grade 3) and hyponatremia (Grade 3) with sodium 123 mmol/L (NR: 134 – 146). On 08 Jan 2015 (Day 58), the study drug was interrupted due to muscular weakness and pain in extremity. The subject was treated with amitriptyline. On 21 Jan 2015 (Day 71), the subject recovered from hyponatremia with sodium 133 mmol/L (NR: 133 – 145) and the study drug was resumed at reduced dose of 4 mg/day due to Investigator decision. The subject was recovering from pain in extremity and did not recover from muscular weakness. The Investigator considered hyponatremia nonserious and possibly related to the study drug; pain in extremity and muscular weakness nonserious and not related to the study drug.

On 23 Jan 2015 (Day 73), the subject fell and was hospitalized on the following day (Day 74) for further evaluation. The subject was diagnosed with spinal cord compression (Grade 3). On 25 Jan 2015 (Day 75), the study drug was interrupted due to this event. On 27 Jan 2015

(Day 77), nuclear magnetic resonance imaging of spine showed spinal cord compression. The subject underwent radiotherapy to thoracic lumbar spine. On 03 Feb 2015 (Day 84), the subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of study drug on 24 Jan 2015 (Day 74). On 11 Feb 2015 (Day 92), the subject recovered with sequelae from spinal cord compression. The Investigator considered spinal cord compression serious and not related to the study drug but related to disease progression.

On 15 May 2015 (Day 185, 111 days after the last dose), the subject died due to clinical disease progression.

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| Subject Number | 17061002 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2016-017525 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Haematuria, Hypomagnesaemia, Hypocalcaemia, Sepsis, Hyperkalaemia (2x) |

A 68-year-old white male was diagnosed with hepatocellular carcinoma on 11 Jun 2015. Significant medical history included arthritis, thrombocytopenia, hemochromatosis, hypothyroidism, musculoskeletal pain (right shoulder pain), and type 2 diabetes mellitus. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amlodipine, atorvastatin, augmentin, avena sativa, bupivacaine, calcium gluconate, canesten-hc, chlorphenamine, gentamicin, ibuprofen, insulin, lekovit ca, levothyroxine, lidocaine, magnesium, metformin, paracetamol, perindopril, piperacillin/tazobactam, quinine, salbutamol, senna alexandrina, triamcinolone, and zopiclone. 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 07 Jul 2015 (Day 1), treatment with study drug was initiated.

On 04 Jun 2016 (Day 334), the subject was hospitalized for hematuria (Grade 2). On 05 Jun 2016 (Day 335), the subject experienced hypocalcemia (Grade 3) and hypomagnesemia (Grade 4). Laboratory tests showed potassium 3.6 mmol/L (NR: 3.5 – 5.1), total calcium 1.55 mmol/L (NR: 2.2 – 2.6), Hgb 126 g/L (NR: 135 – 170), magnesium 0.29 mmol/L (NR: not provided), and platelet count 42 x10^9/L (NR: 140 – 400). Treatment included calcium gluconate, lekovit ca, and magnesium. On 06 Jun 2016 (Day 336), hypomagnesemia improved to Grade 1 and hypocalcemia improved to Grade 2 with calcium 1.97 mmol/L. On 07 Jun 2016 (Day 337), the study drug was interrupted due to hematuria. On the same day (Day 337), the subject experienced sepsis (Grade 4) with underlying cause unknown. Blood cultures were negative. Treatment included piperacillin/tazobactam, gentamicin, and augmentin. On 10 Jun 2016 (Day 340), the subject recovered from hypocalcemia, sepsis, and hematuria, and was discharged from the hospital. On 21 Jun 2016 (Day 351), cystoscopy did not reveal any significant abnormalities. On 28 Jun 2016 (Day 358), the subject recovered from hypomagnesemia. The Investigator considered hematuria serious and possibly related to study drug; hypocalcemia and hypomagnesemia serious (important medical event) and possibly related to study drug; sepsis serious and not related to study drug.

On 27 Jun 2016 (Day 357), the subject was hospitalized for hyperkalemia (Grade 3) with potassium 6.7 mmol/L and creatinine 100 umol/L (NR: 66 – 112) and was treated with calcium gluconate. On the same day (Day 357), hyperkalemia improved to Grade 2 and the subject was discharged from the hospital on 28 Jun 2016 (Day 358) with potassium 5.6 mmol/L. The study drug remained interrupted due to hematuria. The subject did not recover from hyperkalemia. The Investigator considered hyperkalemia serious and not related to study drug.

On 04 Jul 2016 (Day 364), the subject experienced hyperkalemia (Grade 3) with potassium 6.7 mmol/L and the subject was hospitalized on the following day (Day 365). The subject was treated with calcium gluconate, salbutamol, and insulin. On 11 Jul 2016 (Day 371), the study drug was resumed at the same dose. On 01 Aug 2016 (Day 392), the subject recovered from hyperkalemia with the value of potassium 4.2 mmol/L (NR: 3.5 – 5). The Investigator considered hyperkalemia serious and not related to study drug.

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

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| Subject Number | 17071004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-006640 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Hepatic encephalopathy |
| AE(s) Leading to Discontinuation | Hepatic encephalopathy |

A 78-year-old white male was diagnosed with hepatocellular carcinoma in Jun 2013. Significant medical history included alcohol abuse, alcoholic cirrhosis, arthritis (knees), bradykinesia, fatigue, gait disturbance, hypertension, muscle spasms (leg cramps), right portal vein thrombosis, and hands tremor. Previous anticancer therapies included transcatheter arterial chemoembolization (2x). Prior and concomitant medications included acetylsalicylic acid, amlodipine, bisoprolol, omeprazole, quinine, thiamine, and vitamin B complex. 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 08 Apr 2015 (Day 1), treatment with study drug was initiated.

On 14 Apr 2015 (Day 7), the subject experienced hepatic encephalopathy (Grade 1). On 15 Apr 2015 (Day 8), the study drug was interrupted due to hepatic encephalopathy. On 17 Apr 2015 (Day 10), the subject recovered from hepatic encephalopathy. On 21 Apr 2015 (Day 14), laboratory tests were performed and showed ALP 204 U/L (NR: 43 – 115), ALT 46 U/L (NR: 10 – 40), AST 83 U/L (NR: 10 – 43), GGT 380 U/L (NR: 10 – 49), creatinine 44 umol/L (NR: 62 – 124), and total bilirubin 23.6 umol/L (NR: 0 – 18.8). On the same day (Day 14), the study drug was resumed at same dose. The Investigator considered hepatic encephalopathy nonserious and possibly related to the study drug.

On 05 May 2015 (Day 28), the subject was experienced hepatic encephalopathy (Grade 2) and hypertension (Grade 3) with blood pressure of 183/87 mmHg. The subject was treated with amlodipine. Laboratory tests showed ALP 193 U/L, ALT 53 U/L, AST 98 U/L, GGT 315 U/L, creatinine 53 umol/L, and total bilirubin 22.2 umol/L. On 06 May 2015 (Day 29), the subject was hospitalized for hepatic encephalopathy and the study drug was interrupted due to this event. On 07 May 2015 (Day 30), the CT scan of head showed no evidence of bleeding or metastases. On 02 Jun 2015 (Day 56), the subject was withdrawn from the study due to hepatic encephalopathy and received the last dose of the study drug on 05 May 2015 (Day 28). On 21 Jul 2015 (Day 105), the subject recovered from hepatic encephalopathy. The subject did not recover from hypertension. The Investigator considered hepatic encephalopathy serious and possibly related to the study drug and also related to disease progression; hypertension nonserious and probably related to the study drug.

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| Subject Number | 18021007 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-009404 |
| Assigned Treatment | Lenvatinib 12 mg/day |
| Non-Fatal SAE(s) | Bone pain, Metastases to bone, Disturbance in attention |

A 55-year-old white male was diagnosed with hepatocellular carcinoma in Aug 2013. Significant medical history included hypertension, chronic hepatitis B, bilateral renal cyst, hepatic cyst, nephrocalcinosis, and goiter. Previous anticancer therapies included radiotherapy to liver mass (2x; one on each lobe). Prior and concomitant medications included dexamethasone, gabapentin, glucose, hydromorphone, ibuprofen, kalinor-acid, levothyroxine, loperamide, lorazepam, metoclopramide, mirtazapine, movicol, paracetamol, ramipril, tramadol, valoron n, zolpidem, and zopiclone. At Screening, tumor assessments of target/non-target lesions via MRI showed lesions at left liver lobe and unknown site of the bone and liver; mass at left rib. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 30 Jul 2015 (Day 1), treatment with study drug was initiated.

On 30 Jul 2015 (Day 1), the subject experienced bone pain (pain exacerbation osteolytic destruction, ribs, left; Grade 2). On 03 Aug 2015 (Day 5), the subject was hospitalized for worsening of bone pain (Grade 3) and metastases to bone (4th rib; Grade 1). The subject was treated with paracetamol, gabapentin, hydromorphone, and valoron n. On 08 Aug 2015 (Day 10), the severity of bone pain improved to Grade 2. On 19 Aug 2015 (Day 21), the subject experienced disturbance in attention (Grade 2). The subject was treated with dexamethasone and glucose. On 20 Aug 2015 (Day 22), the study drug was interrupted due to disturbance in attention. On 21 Aug 2015 (Day 23), the head CT scan was normal and laboratory tests were not clinically significant. On 22 Aug 2015 (Day 24), the subject recovered from disturbance in attention and was discharged from the hospital. On 25 Aug 2015 (Day 27), the subject recovered from bone pain and metastases to bone. On 27 Aug 2015 (Day 29), the study drug was resumed at same dose. The Investigator considered bone pain, disturbance in attention, and metastases to bone serious and not related to the study drug.

On 08 Oct 2015 (Day 71), the subject experienced diarrhea (Grade 1). On 22 Oct 2015 (Day 85), the event worsened to Grade 3. On the same day (Day 85), the study drug was interrupted due to diarrhea. No treatment was provided. On 29 Oct 2015 (Day 92), the subject recovered from diarrhea. On 05 Nov 2015 (Day 99), the study drug was resumed at a reduced dose of 8 mg/day due to diarrhea. The Investigator considered diarrhea nonserious and probably related to the study drug.

On 04 Jan 2016 (Day 159), tumor response assessment was initially assessed as stable disease which was reevaluated as progressive disease on 11 Jul 2016 (Day 348) after confirmation of scans on 01 Mar 2016 (Day 216). On 10 Mar 2016 (Day 225), the subject was withdrawn from the study due to disease progression and received the last dose of study drug on 09 Mar 2016 (Day 224).

On 15 Jul 2016 (Day 352, 128 days after the last dose), the subject died due to disease progression.

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| Subject Number | 18051004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01476-CLI-DE |
| Assigned Treatment | Lenvatinib 8 mg/day |
| Non-Fatal SAE(s) | Oedema peripheral, Proteinuria |

A 76-year-old white female was diagnosed with hepatocellular carcinoma on 31 Mar 2011. Significant medical history included arteriosclerosis, cardiac failure, cholecystectomy, chronic hepatitis C, hyperthyroidism, aortic valve sclerosis, hepatic cirrhosis, fatigue, flank pain, tobacco user, and intracranial aneurysm. Previous anticancer therapies included hepatectomy, radiofrequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included clonixin, hydrochlorothiazide, metamizole, nifedipine, oxazepam, pantoprazole, ramipril, and spironolactone. At Screening, tumor assessments of target/non-target lesions via CT scan showed mass at left paramediastinal of lung and duodenal lymphadenopathy. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 13 Jan 2014 (Day 1), treatment with study drug was initiated.

On 24 Mar 2014 (Day 71), the subject experienced hypertension (Grade 2) with BP of 150/80 mmHg. On 31 Mar 2014 (Day 78), the subject experienced peripheral edema of the limbs (Grade 2). On 01 Apr 2014 (Day 79), the subject experienced pain in extremity (leg pain; Grade 2). On 08 Apr 2014 (Day 86), the hypertension worsened to Grade 3 with BP 160/90 mmHg and the subject was hospitalized for proteinuria (Grade 2) and peripheral edema of the limbs. The study drug was interrupted due to peripheral edema of the limbs, pain in extremity, and proteinuria. Laboratory results showed BUN 6.07 mmol/L (NR: 1.78 – 7.14), creatinine 62 umol/L (NR: 62 – 124), potassium 4 mmol/L (NR: 3.5 – 5), sodium 144 mmol/L (NR: 133 – 145), urine protein dipstick showed 3+, and the subject's weight was 54 kg (Baseline: 52 kg). The subject was treated with hydrochlorothiazide, clonixin, ramipril, and nifedipine. On 09 Apr 2014 (Day 87), the 24h urine protein was 1.66 g/24hr. On 10 Apr 2014 (Day 88), the chest x-ray showed no effusion or infiltrates; ultrasound of kidney showed normal size kidney with no stenosis; echocardiogram showed slight to moderate aortic valve insufficiency due to sclerosis. On 11 Apr 2014 (Day 89), the subject recovered from peripheral edema of the limbs and pain in extremity and was discharged from hospital. On 22 Apr 2014 (Day 100), the subject recovered from hypertension with blood pressure of 120/60 mmHg. On 05 May 2014 (Day 113), the subject recovered from proteinuria with trace protein on urine dipstick. The Investigator considered peripheral edema of the limbs and proteinuria serious and probably related to the study drug; hypertension nonserious and probably related to the study drug; pain in extremity nonserious and not related to the study drug.

On 05 May 2014 (Day 113), the subject withdrew from study by choice and received the last dose of study drug on 07 Apr 2014 (Day 85).