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| Subject Number | 30161004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01439-CLI-KR |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Back pain |

A 61-year-old Asian male was diagnosed with hepatocellular carcinoma on 05 Nov 2013. Significant medical history included abdominal pain, duodenal ulcer hemorrhage, decreased appetite, back pain, chronic gastritis, chronic hepatitis B, hypertension, left clavicle fracture caused by trauma, and mild splenomegaly. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included amlodipine, chlorphenamine, domperidone, haloperidol, magnesium hydroxide, meteozym, morphine, myprodol, oxycodone, paracetamol, targin, tramadol, trimebutine, and ultracet. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of the liver, pericardium, second lumbar spine metastasis, para-aortic and left supraclavicular lymphadenopathies. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 6.

On 26 Dec 2013 (Day 1), treatment with study drug was initiated.

On 13 Jan 2014 (Day 19), the subject was hospitalized for worsening of back pain (Grade 2). The subject received physical therapy. On 16 Jan 2014 (Day 22), the subject recovered from this event. The study drug dose did not change. The Investigator considered back pain serious and not related to the study drug.

On 14 Feb 2014 (Day 51), tumor response assessment showed disease progression. On 17 Feb 2014 (Day 54), the subject was withdrawn from the study due to disease progression and the last dose of the study drug was received on the same day (Day 54).

On 21 Jun 2014 (Day 178, 124 days after the last dose), the subject died due to unknown reason.

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| Subject Number | 30171008 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2014-002697 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Upper respiratory tract infection |

A 65-year-old Asian male was diagnosed with hepatocellular carcinoma in Jun 2003. Significant medical history included appendicitis, benign prostatic hyperplasia, pulmonary granuloma, colon cancer, diabetes mellitus, esophageal varices, gastric ulcer, gastritis, hepatitis B, herpes zoster, hyperlipidemia, hypertension, chronic gastritis, hepatic cirrhosis, intervertebral disc protrusion, emphysema, renal cyst (both kidneys), and splenomegaly. Previous anticancer therapies included doxorubicin, cisplatin, floxuridine, regional chemotherapy (hepatic intra-arterial chemotherapy), percutaneous ethanol injection therapy, high frequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included alogliptin, amino acids, bifendate, cefodizime, chlorphenamine, cimetropium, ciprofloxacin, cough and cold preparations, dexamethasone, diazepam, epinephrine, general nutrients (geratose), hydrocortisone, lansoprazole, levodropropizine, metformin, metronidazole, morphine, nature's way original primadophilus (lacidofil), oxycodone, paracetamol, pethidine, piperacillin/tazobactam, propacetamol, propranolol, ranitidine, rino ebastel, rosuvastatin, tamsulosin, tenofovir, viscum album, and vitamins with minerals. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver. The BCLC Stage was B, ECOG performance score was 0, and Child Pugh score was 5.

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

On 02 Dec 2014 (Day 76), the subject experienced upper respiratory tract infection (Grade 2) and was treated with diazepam, levodropropizine, paracetamol, and rino ebastel. On 03 Dec 2014 (Day 77), laboratory tests showed WBC 10.67 x10^9/L (NR: 3.5 – 10) and neutrophils 83.7% (NR: 40 – 70). On 23 Dec 2014 (Day 97), the subject was hospitalized for worsening upper respiratory infection (Grade 3) with abdominal pain, chills, vomiting, and temperature of 38.6 ºC. Laboratory tests showed WBC 4.72 x10^9/L and neutrophils 86.7%. The subject was treated with cefodizime, propacetamol, ciprofloxacin, cough and cold preparations, piperacillin/tazobactam, cimetropium, metronidazole, diazepam, levodropropizine, paracetamol, and rino ebastel. On 24 Dec 2014 (Day 98), the study drug was interrupted due to upper respiratory tract infection. On 09 Jan 2015 (Day 114), the subject recovered from upper respiratory tract infection and was discharged from hospital. The Investigator considered upper respiratory tract infection serious and not related to the study drug.

On 30 Dec 2014 (Day 104), tumor response assessment showed disease progression. On 31 Dec 2014 (Day 105), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 23 Dec 2014 (Day 97).

On 13 Feb 2016 (Day 514, 417 days after the last dose), the subject died due to disease progression.

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| Subject Number | 30171010 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-002874 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Abdominal pain |

A 55-year-old Asian female was diagnosed with hepatocellular carcinoma in 2009. Significant medical history included anxiety disorder, cholelithiasis, depression, hepatitis B, hepatic cirrhosis, splenomegaly, and uterine leiomyoma. Previous anticancer therapy included radiofrequency ablation and transcatheter arterial chemoembolization. Prior and concomitant medications included ambroxol, ascorbic acid, betalin complex, clarithromycin, clotiazepam, dexibuprofen, entecavir, escitalopram, hyaluronic acid, hydromorphone, lactulose, megestrol, metoclopramide, morphine, mosapride, paracetamol, pennel, silybum marianum, venlafaxine, and welltamin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of liver and mass in left upper lobe and right lower lobe of lung. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 01 Dec 2014 (Day 53), tumor response assessment showed disease progression. On 04 Dec 2014 (Day 56), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug.

On 24 Dec 2014 (Day 76), the subject was hospitalized for abdominal pain (Grade 3). Treatment included hydromorphone, metoclopramide, and morphine. On 02 Jan 2015 (Day 85), the subject recovered from abdominal pain and was discharged from the hospital on the same day (Day 85). The Investigator considered abdominal pain serious and not related to study drug but related to disease progression.

On 25 Jan 2015 (Day 108, 52 days after the last dose), the subject died due to disease progression.

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| Subject Number | 32041001 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-003479 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Bronchitis |

A 41-year-old Asian male was diagnosed with hepatocellular carcinoma on 20 Mar 2014. Significant medical history included alcoholic cirrhosis and tumor pain. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included actifed, augmentin, ceftazidime, ceftriaxone, cheracol, dextromethorphan, lorazepam, magnesium oxide, panadeine co, potassium, propranolol, ranitidine, sennoside a+b, tramadol, tranexamic acid, and vitamin k. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in right and left lobes of liver and right upper lobe and left lower lobe lung masses. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 04 Apr 2014 (Day 1), treatment with study drug was initiated.

On 10 Apr 2014 (Day 7), the subject experienced palmar-plantar erythrodysesthesia syndrome (Grade 2). On 11 Apr 2014 (Day 8), the study drug was interrupted due to this event. On 17 Apr 2014 (Day 14), the subject recovered from palmar-plantar erythrodysesthesia syndrome. On 18 Apr 2014 (Day 15), the study drug was resumed at the same dose. On 20 Apr 2014 (Day 17), the subject experienced second episode of palmar-plantar erythrodysesthesia syndrome (Grade 2) and the study drug was interrupted due to this event. On 23 Apr 2014 (Day 20), the subject recovered from palmar-plantar erythrodysesthesia syndrome. On 24 Apr 2014 (Day 21), the study drug was resumed at reduced dose of 400 mg/day due to this event. The Investigator considered palmar-plantar erythrodysesthesia syndrome nonserious and probably related to study drug.

On 16 May 2014 (Day 43), the subject was hospitalized for bronchitis (Grade 3) and also had hemoptysis (Grade 2). On 17 May 2014 (Day 44), the subject experienced hypokalemia (Grade 1) and hypomagnesemia (Grade 1). Laboratory tests showed potassium 3.4 mmol/L (NR: 3.5 – 5.1). Treatment included ceftriaxone, dextromethorphan, ceftazidime, augmentin, tranexamic acid, vitamin k, potassium, and magnesium oxide. On 18 May 2014 (Day 45), the study drug was interrupted due to bronchitis and hemoptysis. On the same day (Day 45), the subject recovered from hypokalemia with potassium 3.8 mmol/L. On 21 May 2014 (Day 48), the subject recovered from bronchitis and hemoptysis and was discharged from the hospital. On 22 May 2014 (Day 49), the study drug was resumed at the same dose. On 11 Jun 2014 (Day 69), the subject recovered from hypomagnesemia. The Investigator considered bronchitis serious and not related to study drug; hemoptysis nonserious and not related to study drug but to disease progression; hypokalemia and hypomagnesemia nonserious and not related to study drug.

On 29 May 2014 (Day 56), tumor response assessment showed disease progression. On 11 Jun 2014 (Day 69), the subject was withdrawn from the study due to disease progression and received the last dose on 30 May 2014 (Day 57).

On 24 Jul 2014 (Day 112, 55 days after the last dose), the subject died due to disease progression.

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| Subject Number | 44031004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01406-CLI-SG |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Foreign body, Peripheral swelling (2x), Hepatic failure |

A 68-year-old Chinese male was diagnosed with hepatocellular carcinoma on 05 Feb 2009. Significant medical history included non-cardiac chest pain, hepatitis B, and hypertension. Previous anticancer therapies included hepatectomy (2x) and transcatheter arterial chemoembolization. Prior and concomitant medications included amlodipine, antacids, bisacodyl, bisoprolol, carbohydrates w/fats/levocarnitine/minerals/proteins/taurine/vitamins, ceftriaxone, chlorphenamine, ciprofloxacin, dimeticone, duoderm hydroactive, entecavir, fentanyl, furosemide, glucose, lactulose, loperamide, metronidazole, midazolam, omeprazole, other emollients and protectives (aqueous cream), protein supplements, sennoside a+b, sodium chloride, trimetazidine, vitamin k, and zinc. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left lobe of liver and masses at bilateral lower lobes of lung. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

On 31 Oct 2013 (Day 1), treatment with study drug was initiated.

On 13 Nov 2013 (Day 14), the subject experienced increased blood bilirubin (Grade 3) and proteinuria (Grade 1). Laboratory tests showed total bilirubin 57.6 umol/L (NR: 1.7 – 18.8) and 24h urine protein 0.6828 g/24hr. On 15 Nov 2013 (Day 16), the study drug was interrupted due to increased blood bilirubin and proteinuria. On 26 Nov 2013 (Day 27), the subject recovered from increased blood bilirubin and proteinuria. Repeat total bilirubin was 17.3 umol/L. On 28 Nov 2013 (Day 29), the study drug was resumed at reduced dose of 400 mg/day due to increased blood bilirubin. The Investigator considered increased blood bilirubin and proteinuria nonserious and probably related to study drug.

On 29 Nov 2013 (Day 30), the subject was hospitalized for observation due to foreign body in pharynx (Grade 3) with symptoms of pain. An x-ray of chest and neck showed presence of aluminum package (medication packaging) in pyriform fossa. On 30 Nov 2013 (Day 31), the repeat x-ray revealed that the aluminum packaging was no longer visualized. The subject recovered from foreign body in pharynx and was discharged. The Investigator considered foreign body in pharynx serious and not related to study drug.

On 18 Feb 2014 (Day 111), tumor response assessment showed disease progression. On 20 Feb 2014 (Day 113), the subject was withdrawn from the study due to disease progression and received the last dose on the same day.

On 28 Feb 2014 (Day 121), the subject was hospitalized for peripheral swelling (lower limb swelling; Grade 3). On 01 Mar 2014 (Day 122), doppler ultrasound of both limbs and venous ultrasound showed no deep vein thrombosis. On 02 Mar 2014 (Day 123), the subject

experienced dry skin (Grade 1). Treatment included furosemide, dimeticone, and chlorphenamine. On 03 Mar 2014 (Day 124), the subject recovered from peripheral swelling and dry skin and was discharged from the hospital. The Investigator considered peripheral swelling serious and not related to study drug; dry skin nonserious and not related to study drug.

On 10 Mar 2014 (Day 131), the subject experienced peripheral swelling (lower limb swelling, Grade 1), asthenia (Grade 1), hepatic encephalopathy (Grade 3), and hepatic failure (Grade 3). On 18 Mar 2014 (Day 139), the subject was hospitalized for peripheral swelling. Treatment included ceftriaxone, metronidazole, dimeticone, other emollients and protectives (aqueous cream), and duoderm hydroactive. On 30 Mar 2014 (Day 151, 38 days after the last dose), the subject died due to general physical health deterioration. At the time of death, the subject had not recovered from these events. Autopsy was not performed. The Investigator considered general physical health deterioration, peripheral swelling, and hepatic failure serious and not related to study drug but related to disease progression; hepatic encephalopathy nonserious and not related to study drug but related to disease progression; asthenia nonserious and not related to study drug.

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| Subject Number | 44041001 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01400-CLI-SG |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Cerebrovascular accident |

A 58-year-old Chinese male was diagnosed with hepatocellular carcinoma in Oct 2012. Significant medical history included cough, diabetes mellitus, duodenal ulcer, gastritis, hepatitis B, and esophagitis. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included codeine, domperidone, enoxaparin, entecavir, glibomet, hydrocortisone, linagliptin, mebeverine, promethazine w/codeine, propranolol, rabeprazole, rivaroxaban, triderm, and vildagliptin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe; right hilar lymphadenopathy; right lower and left upper lobe lung masses. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 24 Oct 2013 (Day 56), tumor response assessment showed disease progression.

On 22 Nov 2013 (Day 85), the subject experienced sudden onset of left hand weakness which gradually improved in 90 minutes. The subject was diagnosed with cerebrovascular accident (Grade 2) and the study drug was interrupted. Physical examination showed 4/5 strength in finger extension and 5/5 strength otherwise. On 22 Nov 2013 (Day 85), 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 85). On 23 Nov 2013 (Day 86), the subject was hospitalized for further evaluation. Brain MRI showed multiple acute infarcts of the cerebrum and cerebellum, and trans-esophageal echocardiogram showed thrombus in the pulmonary vein and left atrium. The subject was treated with enoxaparin. On 17 Jan 2014 (Day 141), the subject recovered from cerebrovascular accident. The Investigator considered cerebrovascular accident serious and possibly related to the study drug.

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| Subject Number | 44051002 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01521-CLI-SG |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Sepsis, Tumour haemorrhage, Abdominal pain |

A 47-year-old Chinese male was diagnosed with hepatocellular carcinoma on 09 Sep 2013. Significant medical history included chronic hepatitis B, diarrhea, and lumbar spondylosis. Previous anticancer therapies included radiotherapy to right lobe of liver and hepatectomy. Prior and concomitant medications included ceftriaxone, celecoxib, ciprofloxacin, dextrose and sodium chloride injection, domperidone, entecavir, fentanyl, heparinoid, loperamide, meropenem, metoclopramide, metronidazole, morphine, omeprazole, ondansetron, paracetamol, potassium phosphate monobasic, sangobion, sennoside a+b, sodium chloride, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right lobe of liver, masses at right adrenal and omentum; lymphadenopathy at porta- hepatis. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 6.

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

On 29 Mar 2014 (Day 3), the subject experienced fatigue (Grade 1). On 31 Mar 2014 (Day 5), the study drug was interrupted due to fatigue. On 10 Apr 2014 (Day 15), the subject experienced decreased appetite (Grade 1) and the study drug was resumed at a reduced dose of 400 mg/day due to these events. On 14 Apr 2014 (Day 19), the subject recovered from fatigue and decreased appetite. On 08 May 2014 (Day 43), the subject again experienced fatigue (Grade 1) and decreased appetite (Grade 1). On 09 Jun 2014 (Day 75), the subject recovered from fatigue and decreased appetite. The Investigator considered fatigue, decreased appetite nonserious and possibly related to the study drug.

On 19 May 2014 (Day 54), tumor response assessment showed disease progression. On 22 May 2014 (Day 57), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on the same day.

On 19 May 2014 (Day 54), the subject experienced fistula of small intestine (Grade 3). On 05 Jun 2014 (Day 71), the subject was hospitalized for fistula-related sepsis (Grade 4), gastrointestinal tumor bleeding (Grade 3), and generalized abdominal pain (Grade 3), and also experienced anemia (Grade 3). On 10 Jun 2014 (Day 76), CT mesenteric angiogram did not show intra-abdominal contrast extravasation to suggest active bleeding. Laboratory tests showed RBC 1.99 x10^12/L (NR: 4 – 5.6), WBC 11.2 x10^9/L (NR: 3.7 – 11), Hgb 60 g/L (NR: 125 – 170), Hct 0.185 L/L (NR: 0.37 – 0.51), platelet count 416 x10^9/L (NR: 125 – 375), CRP 118.1 mg/L (NR: 0 – 5), and PT 14.5 sec (NR: 9.4 – 12.5). Blood culture results were not provided. The subject was treated with domperidone, fentanyl, ceftriaxone, meropenem, metronidazole, morphine, packed red blood cell transfusions, paracetamol, and tramadol. On 09 Jun 2014 (Day 75), the subject experienced tachycardia (Grade 3) with a heart rate of 127 bpm, and BP of 114/64 mmHg. On 20 Jun 2014 (Day 86), the subject recovered from

tachycardia and anemia. On 22 Jun 2014 (Day 88), the subject recovered from sepsis, gastrointestinal tumor hemorrhage, and generalized abdominal pain with Hgb 81g/L (NR: 140 – 180), RBC 2.7 x10^12/L (4.6 – 6.3), and WBC 7.37 x10^9/L (NR: 4 – 10). The Investigator considered sepsis, gastrointestinal tumor bleeding, and generalized abdominal pain serious and not related to the study drug but due to disease progression; fistula of small intestine, anemia, tachycardia nonserious and not related to the study drug but due to disease progression.

On 17 Oct 2014 (Day 205, 148 days after the last dose), the subject died due to disease progression.

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| Subject Number | 44051004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01533-CLI-SG |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Colitis, Lower respiratory tract infection, Haematochezia, Haemorrhoids, Pyrexia (2x), Pulmonary embolism, Pneumonia |
| AE(s) Leading to Discontinuation | Pulmonary embolism |

A 62-year-old Chinese male was diagnosed with hepatocellular carcinoma on 23 May 2013. Significant medical history included cholangitis, cholelithiasis, hyperlipidemia, hypertension, and cholestatic jaundice. Previous anticancer therapy included hepatectomy. Prior and concomitant medications included atenolol, augmentin, azithromycin, capiven, ceftriaxone, ciprofloxacin, enoxaparin, hypnotics and sedatives, ibuprofen, lactulose, loperamide, metoclopramide, metronidazole, nifedipine, nystatin, omeprazole, oral colonic lavage, paracetamol, piperacillin/tazobactam, plantago ovata, potassium, proctosedyl, and sodium chloride. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, mass at left lingular lung lobe, and right pleural effusion. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 27 Jun 2014 (Day 19), the subject was hospitalized for colitis (Grade 3), hematochezia (Grade 2), hemorrhoids (Grade 3), lower respiratory tract infection (Grade 3), and pyrexia (non-neutropenic fever; Grade 3). Urine cultures and MRSA screening were negative for any bacterial growth. The subject's body temperature was 39.6 ºC. Laboratory tests showed WBC 4 x10^9/L (NR: 4 – 10), neutrophils 2.84 x10^9/L (NR: 2 – 7.5). The subject was treated with paracetamol, sodium chloride, azithromycin, ceftriaxone, metronidazole, potassium, capiven, ciprofloxacin, and plantago ovata. On 28 Jun 2014 (Day 20), the study drug was interrupted due to hematochezia. On 01 Jul 2014 (Day 23), colonoscopy confirmed hemorrhoid and colitis in rectum. On 03 Jul 2014 (Day 25), the subject recovered from colitis, hematochezia, hemorrhoids, lower respiratory tract infection, and pyrexia. On 07 Jul 2014 (Day 29), the study drug was resumed at the same dose. The Investigator considered colitis, hematochezia, hemorrhoids serious and possibly related to the study drug; lower respiratory tract infection and pyrexia serious and not related to the study drug.

On 24 Jul 2014 (Day 46), the subject was hospitalized for pulmonary embolism (Grade 3) and also experienced peripheral swelling (mild left leg swelling; Grade 1) and pollakiuria (Grade 1). The CT pulmonary angiogram revealed pulmonary embolus in the distal left pulmonary artery extending into the lobar and segmental arteries in the upper and lower lobes, stable pulmonary metastasis, large right pleural effusion, and larger hepatic lesions, suspicious of metastasis. Treatment included enoxaparin, paracetamol, ibuprofen, piperacillin/tazobactam, sodium chloride, potassium, and augmentin. On 24 Jul 2014 (Day 46), the subject was withdrawn from

the study due to the pulmonary embolism secondary to clinical disease progression. The subject received the last dose of the study drug on 24 Jul 2014 (Day 46). On 26 Jul 2014 (Day 48), during hospitalization, the subject experienced pneumonia (Grade 3) and pyrexia (non-neutropenic fever; Grade 3). The chest x-ray showed perihilar infiltrates and right pleural effusion. Blood and urine cultures were negative. On 30 Jul 2014 (Day 52), the subject recovered from peripheral swelling, pollakiuria, pulmonary embolism, pneumonia, and pyrexia. The Investigator considered pulmonary embolism and pyrexia serious and possibly related to the study drug secondary to disease progression; pneumonia serious and possibly related to the study drug; peripheral swelling and pollakiuria nonserious and not related to the study drug.

On 07 Oct 2014 (Day 121, 75 days after the last dose), the subject died due to disease progression.

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| Subject Number | 45011003 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01500-CLI-TW |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Hepatic encephalopathy (2x) |

A 65-year-old Chinese male was diagnosed with hepatocellular carcinoma on 14 Aug 2012. Significant medical history included anemia, chronic hepatitis B, myocardial ischemia, arteriosclerosis coronary artery, duodenal ulcer, gastric ulcer, gastroesophageal reflux disease, cholelithiasis, hypertension, insomnia, skin neoplasm excision (left forearm skin tumor excision), skin neoplasm excision (lip basal cell carcinoma wide excision), hepatic cirrhosis, skin neoplasm excision (nasal basal cell carcinoma excision), extrasystoles, thrombocytopenia, and ventricular extrasystoles. Previous anticancer therapies included percutaneous ethanol injection therapy, radiofrequency ablation, and transcatheter arterial chemoembolization. Prior and concomitant medications included acetylcysteine, alprazolam, ambroxol, amoxicillin, atropine, betamethasone, bisacodyl, calcium gluconate, calcium polystyrene sulfonate, cefixime, cefotaxime, ceftriaxone, clarithromycin, clopidogrel, difenidol, diphenhydramine, entecavir, esomeprazole, fexofenadine, flomoxef, fluticasone, furosemide, fursultiamine w/riboflavin, glucose, haloperidol, human albumin, hydrocortisone, hydroxyzine, hyzaar, insulin, lactulose, lercanidipine, loperamide, lorazepam, magnesium oxide, methylprednisolone, metoclopramide, metronidazole, miconazole, midazolam, morphine, nicorandil, nystatin, pantoprazole, paracetamol, potassium, propranolol, ricinus communis, sennoside a+b, silybum marianum, simeticone, sodium polystyrene sulfonate, spironolactone, strocain, terbutaline, terlipressin, tranexamic acid, triamcinolone, ultracet, and ursodeoxycholic acid. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left and right lobes of liver and masses at bilateral lungs. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 04 Mar 2014 (Day 84), the subject experienced anemia (Grade 2) and the study drug was interrupted due to this event. Laboratory tests showed RBC 2.27 x10^12/L (NR: 4 – 5.6), Hgb 88 g/L (NR: 125 – 170), Hct 0.26 L/L (NR: 0.37 – 0.51). The subject was transfused with packed RBC. On 11 Mar 2014 (Day 91), the subject recovered from anemia. Repeat laboratory tests showed RBC 2.57 x10^12/L, Hct 0.29 L/L, and Hgb 96 g/L (NR: 139 – 191). On 20 Mar 2014 (Day 100), the study drug was resumed at reduced dose of 400 mg/day due to anemia. The Investigator considered anemia nonserious and possibly related to study drug.

On 12 May 2014 (Day 153), the subject was hospitalized for hepatic encephalopathy (Grade 3) with symptoms of intermittent conscious disturbance, incoherent speech, flapping tremor, and ammonia 168 umol/L (NR: 9 – 33). On 13 May 2014 (Day 154), the study drug was interrupted. On the same day (Day 154), the subject experienced portal hypertensive gastropathy (Grade 3) and upper gastrointestinal hemorrhage (Grade 3). Treatment included transfusion with packed RBC, lactulose, and esomeprazole. On 15 May 2014 (Day 156), the subject experienced hypokalemia (Grade 3) with potassium 2.8 mmol/L (NR: 3.5 – 5).

Treatment included potassium. On 19 May 2014 (Day 160), the subject recovered from hepatic encephalopathy and hypokalemia, and was discharged from the hospital. On 27 May 2014 (Day 168), the study drug dose was resumed at a reduced frequency of 400 mg every other day due to hepatic encephalopathy. On the same day (Day 168), the subject recovered from upper gastrointestinal hemorrhage. The subject did not recover from portal hypertensive gastropathy. The Investigator considered hepatic encephalopathy serious and not related to study drug but related to disease progression; upper gastrointestinal hemorrhage nonserious and probably related to study drug; portal hypertensive gastropathy and hypokalemia nonserious and not related to study drug.

On 01 Jul 2014 (Day 203), the subject was hospitalized again for hepatic encephalopathy (Grade 3) with symptom of drowsiness and the study drug was interrupted due to this event. Laboratory tests showed AST 137 U/L (NR: 0 – 39), ALT 222 U/L (NR: 0 – 54), and ammonia 45 umol/L. Treatment included lactulose, sennoside a+b, and bisacodyl. On 09 Jul 2014 (Day 211), the subject withdrew from the study and received the last dose on 30 Jun 2014 (Day 202). The subject did not recover from hepatic encephalopathy and was transferred to hospice care. The Investigator considered hepatic encephalopathy serious and not related to study drug but due to disease progression.

On 05 Aug 2014 (238, 36 days after the last dose), the subject died due to disease progression. Autopsy was not performed.

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| Subject Number | 45041003 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01504-CLI-TW |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Palmar-plantar erythrodysaesthesia syndrome |
| AE(s) Leading to Discontinuation | Fatigue |

A 65-year-old Chinese male was diagnosed with hepatocellular carcinoma on 10 Sep 2013. Significant medical history included corneal leukoma, cholecystectomy, diabetes mellitus, hepatitis B, hepatic cirrhosis, splenomegaly, cataract, keratectomy, and decreased lacrimation. Previous anticancer therapies included hepatectomy and transcatheter arterial chemoembolization. Prior and concomitant medications included acarbose, acetylcysteine, amlodipine, ceftriaxone, clobetasol, dimeticone, esomeprazole, glimepiride, hyoscine, ibuprofen, lidocaine, linagliptin, paracetamol, ultracet, and urea. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at right liver lobe, left upper lung lobe mass, and right hilar lymphadenopathy. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 16 May 2014 (Day 29), the subject was hospitalized for palmar-plantar erythrodysesthesia syndrome (Grade 3) which was accompanied by pyrexia (Grade 1) with body temperature of 37.9 ºC and was treated with ceftriaxone, clobetasol, paracetamol, ultracet, and urea. On the same day (Day 29), the study drug was interrupted due to palmar-plantar erythrodysesthesia syndrome. On 19 May 2014 (Day 32), subject recovered from pyrexia. On 23 May 2014 (Day 36), the subject recovered from palmar-plantar erythrodysesthesia syndrome and the study drug was resumed at a reduced dose of 600 mg/day due to palmar-plantar erythrodysesthesia syndrome. The Investigator considered palmar-plantar erythrodysesthesia syndrome serious and probably related to the study drug; pyrexia nonserious and possibly related to the study drug.

On 16 Jun 2014 (Day 60), the subject experienced fatigue (Grade 3). On 17 Jun 2014 (Day 61), the study drug was interrupted due to fatigue. On 20 Jun 2014 (Day 64), the subject was withdrawn from the study due to fatigue. The subject received the last dose of the study drug on 16 Jun 2014 (Day 60). On 18 Jul 2014 (Day 92), the subject recovered from fatigue. The Investigator considered fatigue nonserious and possibly related to the study drug.

On 08 Aug 2014 (Day 113), tumor response assessment showed disease progression.

On 05 Dec 2014 (Day 232, 172 days after the last dose), the subject died due to disease progression.

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| Subject Number | 45051008 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-004100 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Oesophageal varices haemorrhage (2x) |

A 71-year-old Chinese female was diagnosed with hepatocellular carcinoma on 21 Jul 2014. Significant medical history included hepatitis B, hypertension, coronary artery disease, hepatic cirrhosis, and type 2 diabetes mellitus. Previous anticancer therapies included transcatheter arterial chemoembolization. Prior and concomitant medications included acarbose, acetylcysteine, cefuroxime, chlorphenamine, diosmectite, esomeprazole, glimepiride, human insulin, intravenous solution additives, loperamide, metformin, nifedipine, pantoprazole, platycodon grandiflorus, sodium chloride, somatostatin, tramadol, tranexamic acid, and ultracet. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesion at left lobe of liver and mass in bilateral lower lobes of lung. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

On 08 Dec 2014 (Day –10), the subject had an upper gastrointestinal endoscopy and was found to have esophageal varices (Grade 1), gastroesophageal reflux disease (Grade 1), erosive gastritis (Grade 1), and erosive duodenitis (Grade 1). No treatment was provided. The subject did not recover from these events. The Investigator considered these events nonserious and not related to the study drug.

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

On 28 Dec 2014 (Day 11), the subject experienced maculo-papular rash (Grade 1). On 30 Dec 2014 (Day 13), maculo-papular rash worsened to Grade 3 and was treated with chlorphenamine. On 01 Jan 2015 (Day 15), the study drug was interrupted due to worsening maculo-papular rash. On 08 Jan 2015 (Day 22), maculo-papular rash improved to Grade 1, and the study drug was resumed at reduced dose of 400 mg/day due to maculo-papular rash. On 14 Jan 2015 (Day 28), the subject recovered from maculo-papular rash. The Investigator considered maculo-papular rash nonserious and probably related to the study drug.

On 11 Feb 2015 (Day 56), tumor response assessment showed disease progression. On 16 Feb 2015 (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 15 Feb 2015 (Day 60), the subject was hospitalized for esophageal varices hemorrhage (Grade 3) with symptoms of hemoptysis, bloody vomiting, and tarry stool passage. Laboratory tests showed Hgb 111 g/L (NR: 120 – 160) and stool occult blood 4+. On the same day (Day 60), the subject was transfused with two units of packed red blood cells. Treatment included esomeprazole, pantoprazole, somatostatin, and tranexamic acid. On 16 Feb 2015 (Day 61), the subject experienced gastric ulcer (Grade 1), non-cardiac chest pain (Grade 1), and portal hypertensive gastropathy (Grade 1). The subject was treated with tramadol and ultracet

and had upper gastrointestinal endoscopy and underwent esophageal variceal ligation. On 16 Feb 2015 (Day 61), the subject recovered from non-cardiac chest pain. On 21 Feb 2015 (Day 66), the subject recovered from esophageal varices hemorrhage and was discharged. On 17 Mar 2015 (Day 90), the subject recovered from portal hypertensive gastropathy. The subject did not recover from gastric ulcer. The Investigator considered esophageal varices hemorrhage serious and not related to study drug; gastric ulcer, non-cardiac chest pain, and portal hypertensive gastropathy nonserious and not related to study drug.

On 17 Mar 2015 (Day 90), the subject experienced second episode of esophageal varices hemorrhage (Grade 3) with abdominal pain. Upper gastrointestinal endoscopy showed no blood seen in esophagus, prominent esophageal varices, two ulcers with a white base at antrum and high body, and multiple ulcers in bulb and second portion with hematin coating. Laboratory tests showed Hgb 117 g/L, INR 1.22 (NR: 0.85 – 1.15), and PT 12.6 sec (NR: 8 – 12). Blood pressure was 170/91 mmHg. On 18 Mar 2015 (Day 91), the subject was hospitalized for esophageal varices hemorrhage and underwent esophageal variceal ligation and was treated with cefuroxime. On 23 Mar 2015 (Day 96), the subject recovered from esophageal varices hemorrhage. The Investigator considered esophageal varices hemorrhage serious and not related to study drug.

On 09 Apr 2015 (Day 113, 52 days after the last dose), the subject died due to disease progression.

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| Subject Number | 47011007 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2014-000923 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Hypoacusis |

A 56-year-old Chinese male was diagnosed with hepatocellular carcinoma on 13 Sep 2010. Significant medical history included hepatic cirrhosis, diabetes mellitus, ex-alcoholic, cholelithiasis, sinus bradycardia, and hepatitis B. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included amlodipine, dexamethasone, entecavir, fluocinolone acetonide, gliclazide, loperamide, metformin, other emollients and protectives (aqueous cream), prednisolone, thiamine, and urea. 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 27 Aug 2014 (Day 1), treatment with study drug was initiated.

On 25 Sep 2014 (Day 30), the subject experienced hypoacusis (Grade 3). On 08 Oct 2014 (Day 43), the study drug was interrupted due to this event. On 14 Oct 2014 (Day 49), acoustic stimulation tests showed sensorineural hearing loss of 30 to 70 decibels in right ear. On 16 Oct 2014 (Day 51), the subject received intra tympanic dexamethasone treatment. On 20 Oct 2014 (Day 55), tumor response assessment showed disease progression. On 22 Oct 2014 (Day 57), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on 07 Oct 2014 (Day 42). The CT scan of brain on 04 Nov 2014 (Day 70) did not reveal any brain metastasis. On 10 Nov 2014 (Day 76), the subject recovered from hypoacusis with sequelae. The Investigator considered hypoacusis serious (persistent or significant disability or incapacity) and possibly related to study drug.

On 22 May 2015 (Day 269, 227 days after the last dose), the subject died due to disease progression.

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| Subject Number | 47031011 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-004107 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Back pain |

A 74-year-old Chinese male was diagnosed with hepatocellular carcinoma on 30 Dec 2009. Significant medical history included duodenal ulcer, cholecystectomy, gastritis, hepatitis B, hyperlipidemia, hypertension, central venous catheterization, cholangiostomy (left percutaneous transhepatic biliary drainage), pneumonia, and sepsis. Previous anticancer therapies included hepatectomy and high frequency ablation. Prior and concomitant medications included entecavir, famotidine, hypromellose, ibuprofen, lactulose, nifedipine, paracetamol, liquid paraffin, potassium permanganate, pyridoxine, senna alexandrina, sodium chloride, terazosin, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at left liver lobe and left adrenal mass. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 31 Dec 2014 (Day 14), the subject experienced palmar-plantar erythrodysesthesia syndrome (Grade 3). Treatment included potassium permanganate. On 01 Jan 2015 (Day 15), the study drug was interrupted due to the event. On 14 Jan 2015 (Day 28), palmar-plantar erythrodysesthesia syndrome improved to Grade 2 and pyridoxine was added as a treatment. On 22 Jan 2015 (Day 36), the study drug was resumed at a reduced dose of 600 mg/day due to palmar-plantar erythrodysesthesia syndrome. On 27 Jan 2015 (Day 41), the subject recovered from palmar-plantar erythrodysesthesia syndrome. On 28 Jan 2015 (Day 42), the subject had palmar-plantar erythrodysesthesia syndrome (finger; Grade 1). On 29 Jan 2015 (Day 43), the study drug dose was further reduced to 400 mg/day due to palmar-plantar erythrodysesthesia syndrome. The subject did not recover from palmar-plantar erythrodysesthesia syndrome (finger). The Investigator considered palmar-plantar erythrodysesthesia syndrome and palmar-plantar erythrodysesthesia syndrome (finger) nonserious and probably related to study drug.

On 09 Feb 2015 (Day 54), tumor response assessment showed disease progression. On 11 Feb 2015 (Day 56), 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 56).

On 11 Feb 2015 (Day 56), the subject experienced micturition urgency (Grade 2). On the same day (Day 56), computerized tomography scan of spine showed lytic T12 lesion. On 12 Feb 2015 (Day 57), the subject was hospitalized for back pain (Grade 3). On 13 Feb 2015 (Day 58), nuclear magnetic resonance imaging of spinal cord revealed collapse of T12 which was considered not related to malignant disease, thecal sac indentation at L4/L5 attributed to slight disc herniation, and osteophytes. Treatment included ibuprofen, paracetamol, and tramadol. On 16 Feb 2015 (Day 61), the subject recovered from back pain and was discharged from the hospital. On 17 Feb 2015 (Day 62), the subject experienced hyponatremia (Grade 3) with

sodium 125 mmol/L (NR: 136 – 148) and osteoporosis (Grade 1). Treatment included sodium chloride. On 17 Feb 2015 (Day 62), the subject had splint application for back pain and bladder catheterization for micturition urgency. On 19 Feb 2015 (Day 64), the subject recovered from hyponatremia. On 23 Feb 2015 (Day 68), the subject recovered from micturition urgency. The subject did not recover from osteoporosis. The Investigator considered back pain serious and not related to study drug; osteoporosis, hyponatremia, and micturition urgency nonserious and not related to study drug.

On 18 Sep 2015 (Day 275, 219 days after the last dose), the subject died due to disease progression.

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| Subject Number | 48021003 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | EC-2015-007034 |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Ascites |
| AE(s) Leading to Discontinuation | Ascites |

A 72-year-old Chinese male was diagnosed with hepatocellular carcinoma on 19 May 2014. Significant medical history included diabetes mellitus, hepatitis C, and hypertension. The subject did not receive any previous anticancer therapies. Prior and concomitant medications included antihistamines, augmentin, corticosteroids (dermatological preparations), diphenhydramine, dutasteride, furosemide, human albumin, karvea hct, lidocaine, loperamide, metformin, metoclopramide, paracetamol, propranolol, spironolactone, and terazosin. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right liver lobe. The BCLC Stage was C, ECOG performance score was 1, and Child Pugh score was 5.

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

On 13 May 2015 (Day 330), the subject experienced ascites (Grade 3). Computed tomography scan of abdomen showed gross ascites and the subject was subsequently admitted to the hospital on 20 May 2015 (Day 337) for further evaluation and treatment. Laboratory tests showed albumin 30 g/L (NR: 35 – 55), calcium 1.95 mmol/L (NR: 2.12 – 2.62), BUN 20.35 mmol/L (NR: 1.78 – 7.14), creatinine 239 umol/L (NR: 62 – 124), and total protein 54 g/L (NR: 60 – 80). The subject underwent a CT-guided pigtail catheter insertion to drain the ascites and was also treated with terazosin. On the same day (Day 337), tumor response assessment showed disease progression. On the same day (Day 337), the subject was withdrawn from the study due to ascites secondary to disease progression and on 19 May 2015 (Day 336), the subject received the last dose of the study drug. On 22 May 2015 (Day 339), cytology for ascites fluids was negative for malignant cells. On 23 May 2015 (Day 340), the subject recovered from ascites. The Investigator considered ascites serious and not related to the study drug but related to disease progression.

On 11 Aug 2015 (Day 420, 84 days after the last dose), the subject died due to disease progression.

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| Subject Number | 48051004 |
| Study Name | E7080-G000-304 |
| Eisai Manufacturer's Control Number | E7080-01568-CLI-MY |
| Assigned Treatment | Sorafenib 800 mg/day |
| Non-Fatal SAE(s) | Abdominal pain |

A 47-year-old Asian male was diagnosed with hepatocellular carcinoma on 20 Feb 2014. Significant medical history included diabetes mellitus, hypertension, hepatic cirrhosis, and right upper abdominal pain. Previous anticancer therapy included transcatheter arterial chemoembolization. Prior and concomitant medications included amlodipine, amoxicillin, glycerol, lactulose, metformin, metoprolol, morphine, pantoprazole, perindopril, thymol, and tramadol. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at right lobe of liver, right middle lobe of lung, and right portal vein thrombus. The BCLC Stage was C, ECOG performance score was 0, and Child Pugh score was 5.

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

On 14 Jul 2014 (Day 21), the subject experienced pain in extremity (pain in bilateral soles of feet; Grade 1). On 02 Aug 2014 (Day 40), pain in bilateral soles of the feet increased in severity to Grade 2. On the same day (Day 40), the study drug dose was reduced to 400 mg/day due to this event. The subject was treated with tramadol. On 18 Aug 2014 (Day 56), the subject recovered from pain in extremity. The Investigator considered pain in extremity nonserious and possibly related to the study drug.

On 14 Aug 2014 (Day 52), the subject experienced abdominal pain (Grade 2) with pain around the hypochondrium and the back. The subject was treated with morphine and tramadol. The study drug dose was not changed. On 18 Aug 2014 (Day 56), tumor response assessment showed disease progression. On 02 Sep 2014 (Day 71), the subject was hospitalized for worsening of abdominal pain (Grade 3) with soft and non-tender abdomen. The subject was treated with morphine. Laboratory tests on 15 Sep 2014 showed albumin 38 g/L (NR: 35 – 55), ALP 156 U/L (NR: 43 – 115), AST 25 U/L (NR: 10 – 43), GGT 225 U/L (NR: 10 – 49), absolute neutrophils count 8.5 x10^9/L (NR: 1.7 – 7.9), and potassium 5.4 mmol/L (NR: 3.5 – 5). On 03 Sep 2014 (Day 72), the subject was withdrawn from the study due to disease progression and received the last dose of the study drug on the same day. The subject did not recover from abdominal pain. The Investigator considered abdominal pain serious and not related to the study drug but related to disease progression.

On 02 Nov 2014 (Day 132, 60 days after the last dose), the subject died due to disease progression. Autopsy was not performed.

Eisai 
Protocol: Lenvatinib (E7080) Integrated Summary of Safety

付録 2.7.6.4
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Study 202 - Phase I
Safety Analysis Set

| | Group 1 | | | | | | Group 2 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 12 mg (N=6) | | 16 mg (N=3) | | All (N=9) | | 8 mg (N=6) | | 12 mg (N=5) | | All (N=11) | | All (N=20) | |
| | | Grade >= | | Grade >= | | Grade >= | | Grade >= | | Grade >= | | Grade >= | | Grade >= |
| System organ Class<br>Preferred Term | Any Grade<br>n (%) | 3<br>n (%) | Any Grade<br>n (%) | 3<br>n (%) | Any Grade<br>n (%) | 3<br>n (%) | Any Grade<br>n (%) | 3<br>n (%) | Any Grade<br>n (%) | 3<br>n (%) | Any Grade<br>n (%) | 3<br>n (%) | Any Grade<br>n (%) | 3<br>n (%) |
| Subjects with Any TEAEs | 6 (100.0) | 4 (66.7) | 3 (100.0) | 3 (100.0) | 9 (100.0) | 7 (77.8) | 6 (100.0) | 5 (83.3) | 5 (100.0) | 5 (100.0) | 11 (100.0) | 10 (90.9) | 20 (100.0) | 17 (85.0) |
| 血液およびリンパ系障害 | 3 (50.0) | 0 (0.0) | 2 (66.7) | 1 (33.3) | 5 (55.6) | 1 (11.1) | 5 (83.3) | 2 (33.3) | 2 (40.0) | 0 (0.0) | 7 (63.6) | 2 (18.2) | 12 (60.0) | 3 (15.0) |
| 貧血 | 0 (0.0) | 0 (0.0) | 1 (33.3) | 1 (33.3) | 1 (11.1) | 1 (11.1) | 1 (16.7) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 1 (9.1) | 2 (10.0) | 2 (10.0) |
| 白血球減少症 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (33.3) | 0 (0.0) | 1 (20.0) | 0 (0.0) | 3 (27.3) | 0 (0.0) | 3 (15.0) | 0 (0.0) |
| リンパ球減少症 | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 好中球減少症 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 4 (66.7) | 1 (16.7) | 1 (20.0) | 0 (0.0) | 5 (45.5) | 1 (9.1) | 5 (25.0) | 1 (5.0) |
| 血小板減少症 | 2 (33.3) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 3 (33.3) | 0 (0.0) | 1 (16.7) | 1 (16.7) | 2 (40.0) | 0 (0.0) | 3 (27.3) | 1 (9.1) | 6 (30.0) | 1 (5.0) |
| 心臓障害 | 1 (16.7) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 2 (22.2) | 0 (0.0) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 3 (15.0) | 0 (0.0) |
| 不整脈 | 0 (0.0) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 房室ブロック | 0 (0.0) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 上室性期外収縮 | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 2 (10.0) | 0 (0.0) |
| 耳および迷路障害 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (20.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 耳鳴 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (20.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 内分泌障害 | 0 (0.0) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 2 (10.0) | 0 (0.0) |
| 甲状腺機能亢進症 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 甲状腺機能低下症 | 0 (0.0) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 眼障害 | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 硝子体剥離 | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 胃腸障害 | 6 (100.0) | 0 (0.0) | 3 (100.0) | 0 (0.0) | 9 (100.0) | 0 (0.0) | 6 (100.0) | 2 (33.3) | 5 (100.0) | 1 (20.0) | 11 (100.0) | 3 (27.3) | 20 (100.0) | 3 (15.0) |
| 腹部膨満 | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 0 (0.0) |
| 腹痛 | 2 (33.3) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 3 (33.3) | 0 (0.0) | 3 (50.0) | 0 (0.0) | 2 (40.0) | 0 (0.0) | 5 (45.5) | 0 (0.0) | 8 (40.0) | 0 (0.0) |
| 肛門そう痒症 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 1 (5.0) | 0 (0.0) |

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.0.
TEAE = Treatment-emergent adverse event.

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