Onset Date	September 3, 2015
Past Procedure	Radiotherapy, chemotherapy
Previous Medical History	NA
Current Medical History	Cancer pain, gastritis, peripheral nerve disorder, lymphocytes decreased
Concomitant Medication at Onset of SAE	Amlodipine OD Tablet 5 mg/day, Cardenalin® Tablets 2 mg/day, BIOFERMIN® TABLETS 3 tablets/day, THYRADIN®-S TABLETS 100 μg/day, Takepron® OD Tablets 30 mg/day
Status of the IMP Administration	
Start Date of the IMP Administration	April 21, 2017
Dosage at Onset of SAE	0 mg/day
SAE	
Study Treatment Change	Dose interruption
The Worst Grade	Grade 3
Onset Date of SAE	January 30, 2019
Stop Date of SAE	February 20, 2019
Outcome	Recovering/resolving
Causal Relationship to the IMP	Unrelated
Investigator's Comments on Causality Relationship	This event occurred after start of oral administration of the IMP (lenvatinib); however, the event was diagnosed as an adverse event associated with a condition change of an underlying disease. The event was considered unrelated to the IMP since the IMP administration was interrupted at the time of the event onset. No increase of tumor size was confirmed by CT.
Sequence of Events	
Date	Narrative Text
April 14, 2017	Written informed consent was obtained.
April 20, 2017	The patients was registered to this trial.
April 21, 2017	Lenvatinib 24 mg/day administration started.
May 19, 2017	Scheduled visit. The IMP administration was interrupted due to proteinuria 3+.
May 26, 2017	After confirming that the resumption criteria were satisfied, the IMP administration was resumed with the reduced dose (20 mg) of lenvatinib.
June 9, 2017	Scheduled visit. The IMP administration was interrupted due to proteinuria 3+.
June 14, 2017	After confirming that the resumption criteria were satisfied, the IMP administration was resumed with the reduced dose (14 mg) of lenvatinib.
August 16, 2017	Scheduled visit. The IMP administration was interrupted due to proteinuria 3+.
September 6, 2017	After confirming that the resumption criteria were satisfied, the IMP administration was resumed with the reduced dose (10 mg) of lenvatinib.
January 23, 2019	Scheduled visit. The IMP administration was interrupted due to proteinuria 3+.
January 30, 2019	Unscheduled visit. Proteinuria was negative. The patient was admitted to the hospital for the treatment of pericardial drainage since cough, dyspnea, and weight increased (5 kg) occurred from January 27, and pericardial effusion was confirmed by chest X-ray.
February 1, 2019	Pericardial drainage was started with 600 mL of drainage volume because more effusion was confirmed based on ultrasoundcardiography.
February 2, 2019	Pericardial drainage continued with drainage volume of 15 mL.
February 3, 2019	Pericardial drainage continued with drainage volume of 40 mL.
February 4, 2019	Pericardial drainage continued with drainage volume of 80 mL. Auxocardia and improvement in right pleural effusion was confirmed by chest X-ray. The weight was 60.4 kg.

February 5, 2019	Pericardial drainage was removed.
February 7, 2019	The IMP administration was resumed with the reduced dose (8 mg) of lenvatinib. Since the patient got recovering, she was discharged from the hospital.

9. Subject ID: 1508-011

Subject ID	1508-011
SAE Name	Diarrhoea (investigator term) Diarrhoea (PT)
Demographics	
Sex	Male
Age	6[redacted]
Weight (kg)	52.4
Underlying Disease	
Disease Name (Stage X)	Thymic carcinoma (Stage IVa)
Onset Date	June 1, 2016
Past Procedure	Chemotherapy
Previous Medical History	NA
Current Medical History	Tumor pain, peripheral sensory neuropathy, anemia, pruritus, hyponatremia
Concomitant Medication at Onset of SAE	Cymbalta® Capsules 20 mg/day, Celecox® Tablets 200 mg/day, TRAMCET® Combination Tablets 4 tablets/day, RESTAMIN KOWA CREAM 1%, DEXAN-VG OINTMENT 0.12%, THYRADIN®-S TABLETS 125 μg/day
Status of the IMP Administration	
Start Date of the IMP Administration	May 23, 2017
Dosage at Onset of SAE	14 mg/day
SAE	
Study Treatment Change	Dose interruption
The Worst Grade	Grade 3
Onset Date of SAE	October 13, 2017
Stop Date of SAE	October 16, 2017
Outcome	Recovered/resolved
Causal Relationship to the IMP	Unrelated
Investigator's Comments on Causality Relationship	This diarrhoea accompanied with dehydration required in-hospital care, and was relevant to an SAE; however, the severity of the SAE was determined as Grade 3 and the patient's condition after hospitalization was favorable. At first, the event was considered the causal relationship to the IMP could not be ruled out. However, it was difficult to consider the event related to the IMP because the clinical course would be consistent with the case in which the diarrhoea was caused by meal. Therefore, the causal relationship to the IMP for the diarrhoea was reconsidered unlikely. [Whether to continue participation in this trial or amend the protocol and ICF] Continuation of participation in this trial: possible Amendment of protocol: unnecessary Amendment of ICF: unnecessary
Sequence of Events	
Date	Narrative Text
May 2, 2017	Written informed consent was obtained.
May 22, 2017	The patient was registered to this trial.
May 23, 2017	Lenvatinib 24 mg/day administration started.

May 30, 2017	The IMP administration was interrupted due to Grade 2 intolerable pain.
June 9, 2017	After the pain was resolving, the IMP administration was resumed with the reduced dose (20 mg) of lenvatinib.
June 20, 2017	The IMP administration was interrupted due to Grade 2 intolerable hyperthyroidism.
June 27, 2017	After the hyperthyroidism was resolving, the IMP administration was resumed with the reduced dose (14 mg) of lenvatinib.
October 12, 2017	Scheduled visit of Day 1 in 6th course. None of subjective or objective symptoms, or no abnormal findings in laboratory values were confirmed. Lenvatinib 14 mg/day administration was continued.
October 13, 2017	Unscheduled visit. The patient ate Seared Bonito the day before, and he had 10 or more stools watery from the morning. He had dehydration and was considered to require the in-hospital treatment of Grade 3 diarrhoea. He was admitted to the hospital and the IMP administration was interrupted, and fasting and management with fluid replacement were started.
October 14, 2017	Frequent diarrhoea was improved.
October 15, 2017	Oral intake was resumed.
October 16, 2017	Diarrhoea did not relapse after oral intake was resumed; therefore, management with fluid replacement was discontinued. Diarrhoea was resolved, and the investigator considered that the IMP administration could be resumed in the following day.
October 17, 2017	The IMP administration was resumed with the reduced dose (14 mg) of lenvatinib.

10. Subject ID: 1508-022

Subject ID	1508-022
SAE Name	Urinary tract infection (investigator term) Urinary tract infection (PT)
Demographics	
Sex	Female
Age	6[redacted]
Weight (kg)	63.4
Underlying Disease	
Disease Name (Stage X)	Thymic carcinoma (Stage IVb)
Onset Date	January 28, 2016
Past Procedure	Right thoracoscopic mediastinal tumor/right lobectomy of thymus, radiotherapy, chemotherapy
Previous Medical History	Urinary tract infection, uterine myoma, gallstones
Current Medical History	Hypertension, low back pain, cough, hyperlipidemia, hypoalubuminemia, hyponatremia, sleeplessness, shoulder muscle stiffness, dizziness (ear stone)
Concomitant Medication at Onset of SAE	Nexium® capsules 20 mg/day, Ternelin® Tablets 1.5 mg/day, Dogmatyl® Tablets 150 mg/day, CONSTAN® 0.8 mg. TABLETS 0.8 mg/day, DEPAS® TABLETS 1.5 mg/day, Lendormin® Tablets 0.25 mg/day, Myslee® Tablets 5 mg/day, Amlodipine OD Tablets 10 mg/day, LIVALO TAB. 2 mg/day, CODEINE PHOSPHATE TABLETS 30 mg/day, Mucosolvan® L Tablets 45 mg/day, SELTOUCH® Pap 140 mg/day, THYRADIN®-S TABLETS 60 mg/day, GENTACIN® Ointment 0.1% twice daily
Status of the IMP Administration	
Start Date of the IMP Administration	September 26, 2017
Dosage at Onset of SAE	20 mg/day
SAE	

Study Treatment Change	Dose interruption
The Worst Grade	Grade 3
Onset Date of SAE	November 9, 2017
Stop Date of SAE	November 21, 2017
Outcome	Recovered/resolved
Causal Relationship to the IMP	Unrelated
Investigator's Comments on Causality Relationship	The event was considered unrelated to the IMP because urinary tract infection had repeatedly occurred in the past.
Sequence of Events	
Date	Narrative Text
September 14, 2017	Written informed consent was obtained.
September 26, 2017	Lenvatinib 24 mg/day administration started.
September 27, 2017	Grade 1 general malaise and Grade 1 anorexia occurred.
September 29, 2017	Grade 1 genital itching occurred.
October 3, 2017	General malaise and anorexia was resolved.
October 11, 2017	The patient visited outpatient consultation of dermatology due to genital itching. GENTACIN® application was started in order to treat genital erosion.
October 18, 2017	Grade 1 oral mucositis occurred.
October 23, 2017	Urine protein was 1+.
October 24, 2017	The patient visited outpatient consultation of endocrinology due to 28.08 μIU/mL of TSH. THYRADIN®-S administration was started with Grade 2 hypothyroidism.
October 26, 2017	Grade 1 general malaise and Grade 1 anorexia occurred.
October 31, 2017	The IMP administration was interrupted due to Grade 2 oral mucositis.
November 7, 2017	After oral mucositis was resolved, the IMP administration was resumed with the reduced dose (20 mg) of lenvatinib. Genital itching, general malaise, and anorexia were resolved; urine protein was negative (-).
November 9, 2017	At the evening on November 8, malaise occurred. On November 9, the patient visited the hospital because the malaise worsened and fever occurred. At the outpatient consultation, the following data were collected: Body temperature was 38.0°C, blood pressure was 136/86 mmHg, and pulse rate was 131/min. Rapid influenza diagnostic test: A (-) and B (-) CT: right pleural effusion gently increased but no shadow of pneumonia was observed. Urinalysis (urine dipstick): WBC was 2+, RBC was 2+, and protein was 1+. The patient was admitted to the hospital for the treatment due to pollakiuria (4 times in nighttime and 7 times in daytime) and high-level inflammation with WBC 14,890/μL and CRP 24.52 mg/dL. Urinary tract infection was Grade 3; therefore, SOLYŪGEN G INJECTION and MAXIPIME® FOR INJECTION 4 g/day administration were started.
November 10, 2017	The IMP administration was interrupted. Body temperature was 36.4°C. Concomitant symptoms were resolving such as headache, myalgia, and arthralgia.
November 15, 2017	GPC was 1+ in urine culture. In blood culture, *Bacillus* species and *Staphylococcus epidermidis* were detected.

November 20, 2017	Body temperature was 36.5°C. Urinalysis: negative for urine protein, WBC urine, and urinary occult blood. Hematology: WBC count was 7,590/μL (neutrophil was 82%), platelet count was 513,000/μL, and CRP was 0.85 mg/dL. SOLYŪGEN G INJECTION and MAXIPIME® FOR INJECTION 4 g/day administration were discontinued.
November 21, 2017	Urinary tract infection got Grade 0, and the IMP administration was resumed. The patient was discharged from the hospital.

11. Subject ID: 1508-029 (This SAE was reported in the version.3 SAE report on March 20, 2019.)

Subject ID	1508-029
SAE Name	Pneumonia (investigator term) Pneumonia (PT)
Demographics	
Sex	Male
Age	7[redacted]
Weight (kg)	55.5
Underlying Disease	
Disease Name (Stage X)	Thymic carcinoma (Stage IVb)
Onset Date	July 30, 2013
Past Procedure	Mediastinal tumor resection + combined resection of bilateral pleural tumors + combined resection of pericardium + combined resection of right lung + combined resection of left arm left brachiocephalic vein, radiotherapy, chemotherapy
Previous Medical History	Ureterolithiasis
Current Medical History	Peripheral nerve disorder
Concomitant Medication at Onset of SAE	LOXOPROFEN Na TAPE 100 mg/day, CODEINE PHOSPHATE TABLETS 40 mg/day, Hirudoid® Cream 0.3% 3 times/day, LEVOFLOXACIN OD TABLETS 500 mg/day, Azunol® Gargle liquid 4%, NIFEDIPINE CR TABLETS 40 mg/day, CALONAL® Tab. 200 mg/day
Status of the IMP Administration	
Start Date of the IMP Administration	October 26, 2017
Dosage at Onset of SAE	4 mg/day
SAE	
Study Treatment Change	Dose interruption
The Worst Grade	Grade 3
Onset Date of SAE	February 13, 2019
Stop Date of SAE	March 20, 2019
Outcome	Recovered/resolved
Causal Relationship to the IMP	Related (Version1) Unrelated (Version2 and 3)
Investigator's Comments on Causality Relationship	This event occurred during administration period of the IMP (lenvatinib) and was diagnosed as pneumonia based on chest X-ray result, laboratory test values, and clinical symptoms. This event occurred during the treatment period when the IMP was administered to the patient; however, because no obvious myelosuppression, etc.were observed in the patient at the time of event onset, it was considered to have occurred accidentally rather than to have related to the IMP. Therefore, the event was considered unrelated to the IMP.

Sequence of Events	
Date	Narrative Text
October 25, 2017	Written informed consent was obtained.
October 25, 2017	The patient was registered to this trial.
October 25, 2017	Lenvatinib 24 mg/day administration started.
November 22, 2017	Scheduled visit. The IMP administration was interrupted due to Grade 2 HFS.
November 29, 2017	After confirming that the resumption criteria were satisfied, the IMP administration was resumed with the reduced dose (20 mg) of lenvatinib.
December 20, 2017	Scheduled visit. The IMP administration was interrupted due to fatigue and anorexia.
December 27, 2017	After confirming that the resumption criteria were satisfied, the IMP administration was resumed with the reduced dose (14 mg) of lenvatinib.
January 17, 2018	Scheduled visit. The IMP administration was interrupted due to fatigue and glossitis.
January 24, 2018	After confirming that the resumption criteria were satisfied, the IMP administration was resumed with the reduced dose (10 mg) of lenvatinib.
February 14, 2018	Scheduled visit. The IMP administration was interrupted due to Grade 2 glossitis.
February 28, 2018	The IMP administration was resumed with the reduced dose (8 mg) of lenvatinib.
April 21, 2018	The IMP administration was interrupted due to Grade 2 cheilitis.
May 9, 2018	The IMP administration was resumed with the reduced dose (4 mg) of lenvatinib.
February 13, 2019	The IMP administration was interrupted due to the pneumonia in upper right lobe.
February 20, 2019	Unscheduled visit. The patient was admitted to the hospital for the treatment because the pneumonia in upper right lobe was aggravated. Piperacillin/tazobactam 4.5 g administration started; pyrexia 37.3 degrees, CRP/24.97, WBC/10.6, AST/59, and ALT/45.
February 22, 2019	Pyrexia was resolved and inflammation response was improved. CRP/11.79, WBC/6.4, and AST/150. Changed to ampicillin/sulbactam due to ALT/124 and increased hepatic function. The body temperature ranged 36.0 to 37.1 degrees.
February 25, 2019	CRP/5.32, WBC/6.3, AST/82, and ALT/120. The body temperature ranged 36.5 to 37.0 degrees. Inflammation in clinical findings and hepatic function were observed in improvement.
February 27, 2019	After the patient made steady progress, intravenous drip treatment for him was stopped. CRP/3.13, WBC/7.0, AST/56, ALT/95, and the body temperature ranged 36.5 to 36.9 degrees.
February 28, 2019	Amoxicillin/clavulanate administration started, in good progress.
March 1, 2019	After the patient made steady progress, the patient was discharged from the hospital, and to be followed up on an outpatient basis.
March 6, 2019	Remained opacity in upper right lung lobe was confirmed by chest X-ray but improved. Amoxicillin/clavulanate administration was stopped.
March 20, 2019	SAE was assessed recovered/resolved. Lenvatinib treatment was scheduled to be resumed.

12. Subject ID: 1508-035

Subject ID	1508-035
SAE Name	Pneumothorax (investigator term) Pneumothorax (PT)
Demographics	
Sex	Male

Age	6[redacted]
Weight (kg)	46.4
Underlying Disease	
Disease Name (Stage X)	Thymic carcinoma (Stage IVa)
Onset Date	June 28, 2016
Past Procedure	Chemotherapy
Previous Medical History	NA
Current Medical History	Emphysema, prostatic hypertrophy
Concomitant Medication at Onset of SAE	RELVAR 100 ELLIPTA 30 doses, REBAMIPIDE TABLETS 300 mg/day, URSODEOXYCHOLIC ACID TABLETS 600 mg/day, THYRADIN®-S TABLETS 50 μg/day
Status of the IMP Administration	
Start Date of the IMP Administration	November 16, 2017
Dosage at Onset of SAE	14 mg/day
SAE	
Study Treatment Change	Study treatment discontinuation
The Worst Grade	Grade 3
Onset Date of SAE	May 2, 2018
Stop Date of SAE	July 6, 2018
Outcome	Recovered/resolved
Causal Relationship to the IMP	Unrelated
Investigator's Comments on Causality Relationship	At this point, the details are unclear because the subject is hospitalized in other hospital, but causal relationship to IMP is unlikely because this event was likely to be triggered by coughing from complicated severe emphysema. This event is determined as SAE because the subject needed hospitalization. There is no interaction between other drugs. There is no change in the causal relationship and drug interaction from the previous report. Although the subject has been hospitalized for rehabilitation, the pneumothorax treatment has been completed and the subject's condition is considered to have recovered.
Sequence of Events	
Date	Narrative Text
November 1, 2017	Written informed consent was obtained. The subject had a complication of emphysema.
November 16, 2017	Lenvatinib 24 mg/day administration started.
February 2, 2018	The IMP administration was interrupted for a week due to epigastric discomfort.
February 8, 2018	The IMP administration was resumed with the reduced dose (20 mg) of lenvatinib.
March 23, 2018	The IMP administration was interrupted for a week due to submandibular cellulitis.
March 29, 2018	The IMP administration was resumed with the reduced dose (14 mg) of lenvatinib.

May 2, 2018	The following notification was made from the family member of the subject by phone; the subject had the symptoms of a common cold and coughed for 2 to 3 days. Since yesterday evening, he had complained of chest pain and dyspnea, and made emergency visit to the hospital (Hiroshima City Hiroshima Citizens Hospital, referred the subject to the participating facility). The primary doctor of Hiroshima Citizens Hospital told that the subject was admitted to the hospital due to pneumothorax and started the treatment on this day.
May 23, 2018	Made a phone call to Hiroshima Citizens Hospital to check the subject's condition. Heard that the subject has refractory pneumothorax and not recovered by multiple minocycline pleurodesis. Surgical treatment on May 29, 2018 was being considered.
June 13, 2018	Made a phone call to check the subject's condition. Performed surgical treatment on May 29, 2018, but the drain could not be removed and the subject's condition didn't recover.
June 15, 2018	Requested Patient Referral Document for Hiroshima Citizens Hospital. Informed that study treatment was discontinued because lenvatinib administration failed to be resumed for over the period specified in the study treatment discontinuation criteria of the protocol.
June 28, 2018	Received Patient Referral Document from Hiroshima Citizens Hospital and obtained the following information: On May 2, 2018, chest drainage was performed on the day of emergency admission, but re-expansion of the lung was inadequate. On May 29, 2018, surgical treatment was performed. [VA bullectomy Hybrid (SR:S, IV ics, 5 cm) + Soft thoracoport 12 mm ×2, intercostal nerve block (II to VII) End GIA Black Articulating Reload with Tri-Staple Technology 45 mm Medium/Thick ×1, 3-0 vicryl, fibrin glue 5 mL + PGA Sheet 10 cm (Micro Bubble Method, Reversed Morikawa II Method)] Severe emphysematous changes were showed wholly: multiple pulmonary bullas and perforated part of the lung apex bulla. Lung re-expanded after surgical treatment, but emphysema relapsed. Continuous conservative treatment with glucose and autologous blood was performed and provided adhesion repeatedly. On June 24, 2018, drain was removed because lung expansion was observed on June 21, 2018.
July 6, 2018	Made a phone call to check the subject's condition. The subject was still hospitalized for rehabilitation.