被験者番号	23011003
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	全身健康状態低下/General physical health deterioration，亜イレウス/Subileus
病勢進行による死亡	Yes

A 39-year-old white female was diagnosed with high grade myxoid adipocytic sarcoma in liver on 27 May 2010. The last date of disease progression was 20 Jan 2012. Significant medical history included alopecia, diarrhea, incisional hernia, nausea, resection liver tumor, sarcoma excision, and post-traumatic neck syndrome. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe liver mass at segment 8, splenic mass, small bowel mass and ascites. Previous anticancer therapy included doxorubicin, ifosfamide, and trabectedin. Prior and concomitant medications included cyanocobalamin, erythrocyte transfusion, fentanyl, metoclopramide, morphine, omeprazole, paracetamol, and spironolactone. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 102), the subject was hospitalized for abdominal pain, vomiting, and difficulty in defecation and was diagnosed with subileus (Grade 3). X-ray of abdomen showed ascending, transverse colon and small intestine dilation filled with air fluid levels confirming near total bowel obstruction. The subject underwent insertion of gastric tube and was treated with total parenteral nutrition, meroken and oxycodone. On [redacted] (Day 103), the subject recovered from this event. The Investigator considered subileus serious and not related to the study drug, but probably due to a paracolic tumor mass. The study drug dose was not changed.

On [redacted] (Day 127), the subject was hospitalized for general physical health deterioration (Grade 3) with symptom of worsening ascites and she underwent drainage of ascites. On [redacted] (Day 128), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 113). On [redacted] (Day 130), the subject recovered with sequelae. The Investigator considered general physical health deterioration serious and not related to the study drug, but related to disease progression.

On [redacted] (Day 140, 27 days after last dose), the subject died due to disease progression.

被験者番号	23011007
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	細菌性関節炎/Arthritis bacterial，発熱/Pyrexia，セラチア性菌血症/Serratia bacteraemia

A 58-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 13 Feb 2004. The last date of disease progression was 20 Aug 2012. Significant medical history included hypothyroidism, hysterectomy and right lung lobectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe liver mass, L4 lumbar vertebral lesion and os ilium lesion. Previous anticancer therapy included doxorubicin and pazopanib. Prior and concomitant medications included ibuprofen, levothyroxine, oxycodone and paracetamol. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 27), the subject was hospitalized for bacterial arthritis of right hip (Grade 3). While in the hospital the port-a-catheter infection (Grade 3) was noted. Culture showed staphylococcus aureus positive. On [redacted] (Day 29), the catheter was removed and she was treated with flucloxacillin and the study drug was interrupted. On the same day, the subject recovered from the device related infection. On [redacted] (Day 71), the subject recovered from bacterial arthritis of right hip. The Investigator considered bacterial arthritis of right hip serious and not related to the study drug; device related infection non-serious and not related to the study drug. On [redacted] (Day 43), the study drug was resumed.

On [redacted] (Day 77), tumor response assessment showed disease progression. On [redacted] (Day 86), the subject was withdrawn from the study due to disease progression. The last dose of the study drug was received on [redacted] (Day 71).

On [redacted] (Day 90), the subject was hospitalized due to fever. Blood culture confirmed serratia bacteremia (Grade 3). The subject was treated with amoxicillin/ clavulanic acid and ciprofloxacin. On [redacted] (Day 100), the subject experienced pyrexia (Grade 3) which prolonged hospitalization. She was treated with flucloxacillin and gentamicin. The subject recovered from bacteremia on the same day and from fever on [redacted] (Day 101). The Investigator considered fever and bacteremia serious and not related to the study drug.

被験者番号	24031006
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	肺炎/Pneumonia

A 55-year-old white male was diagnosed with intermediate grade myxoid liposarcoma in right thigh on 05 Apr 2001. The last date of disease progression was 07 Nov 2012. Significant medical history included liver disorder, convulsion, hypoacusis, metastases to retroperitoneum, right thigh surgery (myxoid liposarcoma) and hemipelvectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right inguinal adenopathy and retroperitoneal mass. The subject received previous radiotherapy to right thigh and previous anticancer therapy included doxorubicin, gemcitabine and sirolimus. Prior and concomitant medications included bemiparin, codeine, filgrastim, heparin, levofloxacin and omeprazole. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 20), the subject was hospitalized for pneumonia (Grade 3) associated with cough (Grade 1), dyspnea (Grade 1) and hypotension (Grade 1). The study drug was interrupted due to these events. The subject was treated with paracetamol, ceftazidime and ciprofloxacin. On [redacted] (Day 26), the subject recovered from these events. The Investigator considered pneumonia serious and possibly related to study drug; dyspnea and hypotension non-serious and possibly related to the study drug; and cough non-serious and not related to the study drug. On [redacted] (Day 29), the study drug was resumed.

Sponsor's opinion: Since there was no evidence of neutropenia, the event of pneumonia is unlikely to be related to the study drug.

On [redacted] (Day 43) the subject experienced neutropenia (Grade 4) with absolute neutrophil count of 0.3 x 10^9/L (NR: 1.7-7.9). He was treated with levoflaoxacin and filgrastim and recovered from this event on [redacted] (Day 55). The study drug dose was reduced to 1.1 mg/m2, due to neutropenia. The Investigator considered neutropenia non-serious and possibly related to the study drug.

On [redacted] (Day 83), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 83).

被験者番号	26011009
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	腸閉塞/Intestinal obstruction

A 58-year-old white female was diagnosed with intermediate grade leiomyosarcoma in retroperitoneum on 05 Aug 2011. The last date of disease progression was 13 Mar 2013. Significant medical history included hysterectomy, bilateral salpingo-oophrectomy, and abdominal discomfort. At Screening, tumor assessments of target/non-target lesions via CT scan showed an abdominal mass and left pelvis nodule. Previous anticancer therapy included axitinib, doxorubicin, and palifosfamide. Prior and concomitant medications included dexamethasone, electrolytes with macrogol, lansoprazole, salicylic acid, and tetanus vaccine. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 76), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 71).

On [redacted] (Day 80), the subject was hospitalized due to intestinal obstruction (Grade 3), associated with vomiting (Grade 3) and constipation (Grade 3). She was treated with paracetamol, morphine, electrolytes with macrogol and metoclopramide. She recovered from vomiting on [redacted] (Day 93) and did not recover from constipation. She recovered from intestinal obstruction with sequelae (subacute obstruction, no further episodes) on [redacted] (Day 105). The Investigator considered intestinal obstruction serious and not related to the study drug; vomiting and constipation non-serious and not related to the study drug.

被験者番号	26031003
投与群	本薬群：1.4 mg/m² IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	発熱/Pyrexia

A 63-year-old white male was diagnosed with high grade leiomyosarcoma in stomach on 17 Feb 2008. The last date of disease progression was 15 Jun 2012. Significant medical history included functional cardiac murmur, hypertension, laparotomy, decreased hemoglobin, small intestine carcinoma, mitral valve incompetence, pyrexia's of unknown origin, gastric disorder and type 2 diabetes mellitus. At Screening, tumor assessments of target/non-target lesions via CT scan showed retroperitoneal mass. Previous anticancer therapy included doxorubicin, gemcitabine, trabectedin, and docetaxel. Prior and concomitant medications included amitriptyline, ciprofloxacin, dexamethasone, domperidone, electrolytes with macrogol, fluconazole, ibuprofen, lisinopril, loperamide, nystatin, omeprazole, prednisolone, red blood cells, and stomatologicals. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 16), the subject was hospitalized for pyrexia (Grade 3) with hemoglobin of 91g/L (NR: 125-170 g/L); hematocrit of 26.6 % (NR: 35-51%) and temperature of >38 degree Celsius (NR: 36.5 – 37.2). The subject was transfused with 2 units of red blood cells. On [redacted] (Day 17), the subject recovered from pyrexia. The Investigator considered pyrexia serious and possibly related to the study drug. .

On [redacted] (Day 40), the subject was again hospitalized due to pyrexia (Grade 3). The subject had a PICC line inserted four days prior to the onset of the event. Two days prior, the subject had symptoms of lethargy, poor oral intake and urinary frequency. He underwent blood tests, blood cultures, chest x-ray, urine dipstick and culture and sensitivity with unknown results. He was treated with meropenem, teicoplanin, enoxaparin, phosphate sandoz, ciprofloxacin and calcium carbonate. The subject recovered on [redacted] (Day 44). The Investigator considered pyrexia serious and not related to the study drug. The study drug dose was not changed

On [redacted] (Day 78), the subject experienced pyrexia (Grade 1). On [redacted] (Day 80), the subject was hospitalized due to pyrexia (Grade 2). He was treated with meropenem, teicoplanin, enoxaparin, phosphate sandoz, ciprofloxacin and calcium carbonate. The subject recovered on [redacted] (Day 84) from pyrexia. The Investigator considered pyrexia serious and not related to the study drug.

On [redacted] (Day 86), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 93).

被験者番号	32041002
投与群	本薬群：1.4 mg/m² IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	低ナトリウム血症/Hyponatraemia

A 73-year-old asian female was diagnosed with intermediate grade leiomyosarcoma in retroperitoneum on 26 Nov 2010. The last date of disease progression was 27 Dec 2012. Significant medical history included constipation, hypertension, pelvis pain, and spondylolisthesis. At Screening, tumor assessments of target/non-target lesions via CT scan showed retroperitoneal mass and liver mass on segments 5, 7 and 8. Previous anticancer therapy included cisplatin, cylophosphamide, doxorubicin, and etoposide. Prior and concomitant medications included amlodipine, bisacodyl, dexamethasone, dextran, lorazepam, magnesium, magnesium hydroxide, magnesium sulfate, ondansetron, senna alexandrina, sodium chloride and tramadol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 8), the subject experienced leukopenia (Grade 3) with WBC count of 1.7 10^9/L (NR: 3.7-11), neutropenia (Grade 2) with neutrophils count of 1.2 x 10^9/L (NR: 1.7 – 7.9) and hyponatremia (Grade 1) with sodium level of 132.7 mmol/L (NR: 133-145). On [redacted] (Day 15), the event of leukopenia improved to grade 1. On the same day, the study drug dose was reduced to 1.1 mg/m² due to leukopenia. On [redacted] (Day 22), the events of hyponatremia and neutropenia recovered. The subject did not recover from leukopenia. The investigator considered hyponatremia, leukopenia and neutropenia non-serious and possibly related to the study drug.

On [redacted] (Day 30), the subject was hospitalized due to hyponatremia (Grade 3) with sodium level of 123.4 mmol/L. The study drug was interrupted due to hyponatremia. She was treated with sodium chloride. On [redacted] (Day 36), the hyponatremia improved to Grade 1 and the study drug was resumed at the same dose. On [redacted] (Day 43), the subject experienced hyponatremia (Grade 3) with sodium level of 128 mmol/L. On the same day her leukopenia worsened to grade 2 with WBC counts 2.3 x 10^9/L. She was treated with sodium chloride and recovered from hyponatremia on [redacted] (Day 152) with the sodium level of 135 mmol/L. The subject recovered from leukopenia on [redacted] (Day 60). The Investigator considered hyponatremia serious and not related to the study drug; leukopenia non-serious and possibly related to the study drug.

On [redacted] (Day 39), tumor response assessment showed disease progression and the subject was withdrawn from the study on [redacted] (Day 60). The subject received the last dose of the study drug on [redacted] (Day 43).

被験者番号	35011002
投与群	本薬群：1.4 mg/m² IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	アラニンアミノトランスフェラーゼ増加/Alanine aminotransferase increased, アスパラギン酸アミノトランスフェラーゼ増加/Aspartate aminotransferase increased, 胆管拡張/Biliary dilatation

A 28-year-old asian male was diagnosed with high grade leiomyosarcoma in retroperitoneum on 30 Jun 2008. The last date of disease progression was 10 Apr 2012. Significant medical history included, back pain, constipation and retroperitoneal biopsy. At Screening, tumor assessments of target/non-target lesions via CT scan showed intrahepatic liver mass at S5, and right upper lobe liver nodule. Previous anticancer therapy included doxorubicin, cisplatin, ifosfamide, gemcitabine, and docetaxel. Prior and concomitant medications included acetylcysteine, ceftriaxone, clinimix, dexamethasone, eperisone, furosemide, heparin, hyoscine, magnesium oxide, magnesium sulfate, metoclopramide, metronidazole, morphine, multitrace-4, oxycodone, palonosetron, pethidine, ranitidine, sodium bicarbonate, sucralfate, ulinastatin, vitamins and zolpidem. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 9), the subject experienced neutropenia (Grade 2) with absolute neutrophil counts of 1.3 x 10^9/L (NR: 1.7 – 7.9) which recovered on [redacted] (Day 28). On [redacted] (Day 36), the subject again experienced neutropenia (Grade 3) with an absolute neutrophil count of 0.96 x 10^3/uL. He recovered from this event on [redacted] (Day 42). On [redacted] (Day 43), the study drug was reduced to 1.1 mg/m^2 due to neutropenia. The Investigator considered this event non-serious and probably related to the study drug.

On [redacted] (Day 53), the subject was hospitalized due to biliary dilatation (Grade 3). Laboratory results showed AST of 38 IU/L (NR: 10-43); ALT of 34 IU/L (NR: 10-43) and alkaline phosphatase of 124 IU/L (NR: 43-115). He was treated with ciprofloxacin, general nutrients, multitrace-4, diosmectite, glucose, metoclopramide, and hartman's solution. The subject recovered from this event on [redacted] (Day 56). The Investigator considered this event serious and not related to the study drug. The study drug dose was not changed.

On [redacted] (Day 274), the subject experienced increased alanine aminotransferase (ALT) (Grade 1) and increased aspartate aminotransferase (AST) (Grade 1) with ALT of 88 IU/L (10-40 U/L) and AST of 70 IU/L (NR: 10-43 U/L) . On [redacted] (Day 295), the subject was hospitalized for increased AST (Grade 2) and increased ALT (Grade 2) with AST of 162 IU/L and AST of 157 IU/L. He was treated with flavine adenine dinucleotide, godex, uresodeoxycholic acid and ornithine. He recovered from these events on [redacted] (Day 311). The Investigator considered these events serious and not related to the study drug.

On [redacted] (Day 297), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 281).

被験者番号	35061012
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	イレウス/Ileus

A 50-year-old asian female was diagnosed with high grade leiomyosarcoma in uterus on 22 Oct 2007. The last date of disease progression was 14 Jan 2013. Significant medical history included gastroenteritis clostridial, debridement, appendicectomy, mass excision (peritoneum mesentery), colectomy, paraaortic lymph gland biopsy, lymphadenectomy (pelvis), pelvic adhesiolysis, urethral pain, omentectomy, lymph node tuberculosis, ureteric repair, urinary tract infection enterococcal, and wound closure. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lower lobe lung mass, abdominal mass, liver mass and peritoneal seeding. Previous anticancer therapy included cisplatin, doxorubicin, docetaxel and gemcitabine. Prior and concomitant medications included albumin, amino acids, amino acids with calcium chloride/electrolytes, bisacodyl, calcium carbonate, cefepime, ceftriaxone, chlorhexidine, fentanyl, filgrastim, fravasole, furosemide, ketorolac, lactulose, magnesium oxide, metoclopramide, metronidazole, morphine, oxycodone, paracetamol, piperacillin, piroxicam, potassium, propacetamol, ramosetron, red blood cells, solifenacin, tamsulosin, tobramycin, tramadol, tranexamic acid, ultracet, and vitamins. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 7), the subject experienced abdominal pain (Grade 1). Her treatment included morphine, ketorolac, paracetamol, tramadol, oxycodone, and fentanyl. The subject recovered from abdominal pain on [redacted] (Day 21). The Investigator considered abdominal pain non-serious and not related to the study drug.

On [redacted] (Day 3), the subject was hospitalized with fever and abdominal pain. Abdominal x-ray confirmed ileus (Grade 2). She was treated with albumin and furosemide and a nasogastric tube (Levin) was inserted. On [redacted] (Day 7), the subject was found to have abdominal distension (Grade 1), constipation (Grade 1) and nausea (Grade 1). She was treated with lactulose, magnesium oxide and bisacodyl. She recovered from nausea on the same day and from constipation on [redacted] (Day 12) and did not recover from abdominal distension and ileus. The Investigator considered ileus serious and not related to study drug but due to disease progression; abdominal distension, constipation and nausea non-serious and not related to the study drug.

On [redacted] (Day 13), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 7).

被験者番号	41011001
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	貧血/Anemia, 肺炎/Pneumonia, 尿路感染/Urinary tract infection

A 55-year-old white female was diagnosed with intermediate grade liposarcoma in connective and soft tissue of right thigh on 25 Jul 2011. The last date of disease progression was 14 Mar 2012. Significant medical history included back pain, anemia, hyperlipidaemia, right leg edema and superficial thrombophlebitis (right leg). At Screening, tumor assessments of target/non-target lesions via CT scan showed left adrenal mass, colorectal mass, right kidney mass and lesions in posterior upper and lower right soft tissue trunk,and extremity, abdomen muscles, and right breast. Previous anticancer therapy included doxorubicin and ifosfamide. Prior and concomitant medications included alprazolam, enoxaparin, fentanyl, gabapentin, ibuprofen, mirtazapine, oxycodone, and sodium chloride. ECOG performance status at screening was 2.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 84), the subject was admitted to the hospital for urinary tract infection (Grade 2) and anemia (Grade 2) with hemoglobin of 84 g/L (NR: 110-155). She was transfused with red blood cells and plasma and treated with norfloxacin. On the same day, tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 71). On [redacted] (Day 91), the subject recovered with sequelae from urinary tract infection and the outcome of anemia was unknown. The Investigator considered urinary tract infection and anemia serious and not related to the study drug.

On [redacted] (Day 84), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 71).

On [redacted] (Day 101), the subject was hospitalized for pneumonia (Grade 4). On [redacted] (Day 105, 35 days after the last dose), the subject died of pneumonia secondary to disease progression. The Investigator considered pneumonia serious and not related to the study drug.

被験者番号	41011004
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	好中球減少症/Neutropenia

A 41-year-old white female was diagnosed with high grade leiomyosarcoma in bones and joints in the right lower leg on 05 May 2011. The last date of disease progression was 20 Jul 2012. Significant medical history included biopsy of leiomyosarcoma, and bromexin allergy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe lung mass and liver mass. Previous anticancer therapy included doxorubicin, ifosfamide and trabectedin. Prior and concomitant medications included red blood cells. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15), the subject experienced neutropenia (Grade 4) with neutrophil count of 0.12x10^9/L (NR: 1.7 – 7.9). She was treated with filgrastim, nifuroxazide, fluconazole and ciprofloxacin. On [redacted] (Day 17), she recovered from neutropenia. On [redacted] (Day 22), the study drug dose was reduced to 1.1 mg/m^2. The Investigator considered neutropenia serious (important medical event) and probably related to the study drug.

On [redacted] (Day 29), the subject experienced neutropenia (Grade 3) with neutrophil counts 0.81x10^9/L. She was treated with filgrastim, ciprofloxacin and fluconazole. She recovered from neutropenia on [redacted] (Day 30). On the same day, the study drug dose was reduced to 0.7 mg/m^2. The Investigator considered neutropenia serious (important medical event) and possibly related to the study drug.

On [redacted] (Day 36) the subject experienced another episode of neutropenia (Grade 3) with neutrophil count of 0.99 x 10^9/L. She was treated with filgrastim and recovered from this event on [redacted] (Day 43). The Investigator considered this event non-serious and possibly related to study drug.

On [redacted] (Day 44), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 43).

被験者番号	41031003
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	気管支肺炎/Bronchopneumonia，発熱/Pyrexia

A 56-year-old white female was diagnosed with intermediate grade leiomyosarcoma in smooth muscle of the thigh on 06 Aug 2008. The last date of disease progression was 12 Jan 2012. Significant medical history included, hip arthroplasty, sarcoma excision, and right leg varicose vein operation. At Screening, tumor assessments of target/non-target lesions via CT scan showed right left upper lobe lung mass. The subject received previous radiotherapy to lung mass and right lower lobe mass and previous anticancer therapy included doxorubicin, ifosfamide and trabectedin. Prior and concomitant medications included alprazolam, ambroxol, ciprofloxacin, clarithromycin, diazepam, filgrastim, ibuprofen, lactobacillus helveticus, metamizole, mirtazapine, ondansetron, paracetamol, sodium chloride, thiethylperazine and zolpidem. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 43), subject was hospitalized with suspected bilateral bronchopneumonia (Grade 3) associated with cough and mild fever. She underwent chest X-ray and chest CT scan which confirmed the diagnosis. She was treated with amoxicillin-clavulanic acid, augmentin, ambroxol and paracetamol and recovered from bronchopneumonia on [redacted] (Day 57). The Investigator considered this event serious and possibly related to the study drug. On [redacted] (Day 64), the study drug dose was reduced to 1.1 mg/m^2 due to this event.

On [redacted] (Day 107), the subject was hospitalized for pyrexia (Grade 1) of 39 degree celsius (NR: 36.5 – 37.2). On [redacted] (Day 112), she experienced neutropenia (Grade 4) with neutrophil count 0.4 x 10^9/L (NR: 1.7 – 7.9) and leukopenia (Grade 3) with WBC count of 1.670 x 10^9/L (NR: 3.7 – 11). She was treated with plasmalyte, codeine, filgrastim and paracetamol and recovered from these events on [redacted] (Day 114). On [redacted] (Day 120), the study drug dose was reduced to 0.7 mg/m^2. The Investigator considered pyrexia serious and possibly related to the study drug; neutropenia and leukopenia non-serious and probably related to the study drug.

On [redacted] (Day 148), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 140).

被験者番号	41031005
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	尿路感染/Urinary tract infection
治験薬の投与中止に至った有害事象	尿路感染/Urinary tract infection

A 64-year-old white female was diagnosed with intermediate grade adipocytic myxoid sarcoma in retroperitoneum and inguinal area on 09 Nov 2006. The last date of disease progression was 10 Jan 2013. Significant medical history included type 2 diabetes mellitus, hypothyroidism, borrelia infection, extirpation in retroperitoneum and inguinal, umbilical hernia repair, hysterosalpingo-oophorectomy, laparotomy, pulmonary embolism and retroperitoneal cyst removal. At Screening, tumor assessments of target/non-target lesions via CT scan showed omental mass, retroperitoneal lymph node lesions, peritoneum-pelvic lesions, and pelvic lesions. Previous anticancer therapy included ifosfamide and doxorubicin. Prior and concomitant medications included acetylcysteine, augmentin, baralgina, bromazepam, butamirate, dynamag, famotidine, lactobacillus helveticus, levothyroxine, metamizole, metformin, metoclopramide, nadroparin, nimesulide, nitrofurantoin, omeprazole, ondansetron, paracetamol, stoptussin, thiethylperazine, tramadol, vitamin b complex and zolpidem. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 407), the subject experienced urinary tract infection (Grade 2). She was treated with cefuroxime and ciprofloxacin and recovered from this event on [redacted] (Day 437). On [redacted] (Day 442) the subject was hospitalized for urinary tract infection (Grade 3). She underwent an ultrasound of kidney and J-J stent placement in the left ureter. The subject was treated with cefuroxime and ciprofloxacin and recovered from urinary tract infection on [redacted] (Day 448). On the same day, the subject was withdrawn from the study due to urinary tract infection secondary to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 428). The Investigator considered urinary tract infection serious and not related to the study drug but to progressive disease.

被験者番号	44041005
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	高ビリルビン血症/Hyperbilirubinaemia, 腸閉塞/Intestinal obstruction
病勢進行による死亡	Yes

A 50-year-old white female was diagnosed with high grade leiomyosarcoma in corpus uteri on 20 Sep 2011. The last date of disease progression was 27 Mar 2013. Medical history included alopecia, total hysterosalpingo-oophorectomy and hydronephrosis. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in left obturator lymph node, abdominal and pelvic adenopathy, pelvic mass and left lateral lobe liver mass. Previous anticancer therapy included docetaxel, doxorubicin, gemcitabine, ifosfamide and paclitaxel. Prior and concomitant medication included potassium. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 8), the subject was hospitalized for hyperbilirubinemia (Grade 4) with total bilirubin of 172.4 uMol/L (NR: 1.7 – 18) and intestinal obstruction (Grade 4). The subject was also found to have neutropenia (Grade 3), hypocalcaemia (Grade 3), anemia (Grade 2) and cachexia (Grade 2). Laboratory tests showed WBC count of 3.1 x 10^9/L (NR: 3.7 – 11), hemoglobin 81 g/L (NR: 110-155), hematocrit 25.3% (NR: 33 -47) and calcium 1.62 mmol/L (NR: 2.12 – 2.62). On the same day, the subject was withdrawn from the study due to clinical disease progression. The last dose of the study drug was received on [redacted] (Day 1). On [redacted] (Day 10), the subject underwent right ileostomy which revealed abdominal and pelvic obstruction above the level of the umbilicus involving loops of the small intestine and colon, peritoneal carcinomatosis, carcinomatous ascites and multiple hepatic metastases. On [redacted] (Day 11), the subject experienced postsurgical evisceration (Grade 2). The subject did not recover from these events and was discharged from the hospital per family's request on [redacted] (Day 23). The Investigator considered hyperbilirubinemia and intestinal obstruction serious and not related to the study drug; wound evisceration, hypocalcemia, cachexia non-serious and not related to the study drug; neutropenia non-serious and probably related to study drug and anemia non-serious and possibly related to the study drug.

On [redacted] (Day 30, 29 days after last dose), the subject died due to disease progression.

被験者番号	46031002
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	貧血/Anemia，好中球減少症/Neutropenia，発熱/Pyrexia，小腸閉塞/Small intestinal obstruction，ブドウ球菌性菌血症/Staphylococcal bacteremia，腫瘍熱/Tumor associated fever

A 53-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 13 Aug 2008. The last date of disease progression was 29 Nov 2011. Significant medical history included tumor fever, anemia, hydronephrosis, kidney infection, arthralgia, lymphadenectomy, ureterolysis procedure, hydronephrosis, nephrostomy, lung neoplasm surgery, hysterosalpingo-oophorectomy, urinary tract infection, and uterine leiomyoma. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in soft tissue trunk. The subject received previous radiotherapy to pelvis. Previous anticancer therapy included docetaxel, doxorubicin, gemcitabine, ifosfamide, and trabectedin. Prior and concomitant medications included bisacodyl, diphenhydramine, exemestane, furosemide, glucose, hydrocortisone, metamizole, metoclopramide, micolette, morphine, osmotan, oxycodone, pamidronic acid, paraffin, liquid, pregabalin, promethazine, ranitidine, sodium chloride, and targin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 24), the subject was hospitalized for fever (Grade 1), staphylococcal bacteremia (Grade 4) and anemia (Grade 2) with hemoglobin of 95 g/L (NR: 110 -155). She underwent blood transfusion and was treated with metamizole, naproxen and paracetamol. On [redacted] (Day 25), the subject experienced rash due to blood transfusion (Grade 2). She was treated with hydrocortisone and promethazine. She recovered from anemia on [redacted] (Day 26) and from fever and rash on [redacted] (Day 27). On [redacted] (Day 29), she experienced neutropenia (Grade 4) with neutrophil count 0.2 x 10^9/L (NR: 1.7 – 7.9) and was diagnosed with tumor associated fever (Grade 1) and decreased white blood cell count (Grade 3) with WBC of 1.5 x 10^9/L (NR: 3.7 -11 (x10^9/L). Repeat culture from port catheter showed Staphylococcus infection (Grade 4). The study drug was interrupted due to staphylococcal bacteremia and decreased and never resumed. She was treated with vancomycin and cefazolin. On [redacted] (Day 30), she anemia recurred (Grade 2) with hemoglobin of 96.4 g/L and underwent transfusion of two units of blood. On [redacted] (Day 25), neutropenia improved to Grade 3 with neutrophil count 0.57 x 10^9/L which further improved to Grade 2 on [redacted] (Day 33) with neutrophil count 1.1 x 10^9/L. She recovered from decreased white blood cell count on [redacted] (Day 35) and from neutropenia on [redacted] (Day 34). She experienced another rash due to blood transfusion (Grade 2) and was treated with promethazine and diphenhydramine and recovered from rash on the same day. On [redacted] (Day 43), the subject recovered from staphylococcal bacteremia and tumor associated fever. The Investigator considered fever, neutropenia and anemia serious and probably related to the study drug; tumor associated fever and staphylococcal bacteremia serious and not related to the study drug; rash non-serious and not related to the study drug; decreased white blood cell count non-serious and possibly related to the study drug.

On [redacted] (Day 44), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of study drug on [redacted] (Day 22).

On [redacted] (Day 51), the subject was hospitalized due to vomiting, abdominal pain, bloating and stomach gas. She was diagnosed with small intestinal obstruction (Grade 3) and treated with morphine, hyoscine, osmotan and metamizole. On [redacted] (Day 62), she underwent segmental small bowel resection, anastomosis and retroperitoneal mass resection. On the same day, she recovered from this event. The Investigator considered small intestinal obstruction serious and not related to the study drug, but related to underlying condition.

被験者番号	46041008
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	医療機器関連感染/Device related infection

A 55-year-old white male was diagnosed with high grade leiomyosarcoma in gum, floor of mouth, and nose on 28 Dec 2009. The last date of disease progression was 17 Jun 2012. Significant medical history included chronic obstructive pulmonary disease, type 1 diabetes mellitus, diabetic retinopathy, metastases to lungs, neuralgia, asthma, cervical lymph node palpable, drug allergy to aredia, and severe cough. At Screening, tumor assessments of target/non-target lesions via CT-showed right lower lobe lung mass and left femur (soft tissue) lesion. The subject received previous radiotherapy to left femur bone and maxilla. Previous anticancer therapy included doxorubicin, ifosfamide and trabectedin. Prior and concomitant medications included glucerna, amoxicillin, fentanyl, gabapentin, insulin glargine, insulin lispro, metamizole, naproxen, omeprazole, salbutamol, sildenafil and targin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 23), the subject was found to have fever for four days which subsided spontaneously. After opening port-a-cath at the hospital, the subject experienced fever (Grade 2) with chills. Cultures from port showed positive for Rhizobium radiobacter and Klebsiella pneumonia; peripheral blood sample showed positive for Rhizobium radiobacter. The subject was diagnosed with device related infection (Grade 2). He was treated with ceftriaxone, ceftazidime, cefuroxime and ciprofloxacin. On [redacted] (Day 24), the subject recovered from fever. On [redacted] (Day 30), infected port-a-cath was removed and he recovered from infection on [redacted] (Day 31). The Investigator considered device-related infection serious and not related to study drug; fever non-serious and not related to study drug.

On [redacted] (Day 148), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 121).

被験者番号	47031003
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	背部痛/Back pain

A 32-year-old white female was diagnosed with intermediate grade adipocytic round cell in retroperitoneum (back paraspinal) on 21 May 2004. The last date of disease progression was 01 Feb 2013. Significant medical history included tumor pain, paraparesis, osteomyelitis and multiple tumor excisions. At Screening, tumor assessments of target/non-target lesions via MRI showed extramedullary intraspinal lesions. The subject received previous radiotherapy to soft tissue tumor bed. Previous anticancer therapy included doxorubicin, ifosfamide, and trabectedin. Prior and concomitant medications included alprazolam, bisacodyl, bisoprolol, cefalexin, ciprofloxacin, clindamycin, clonazepam, clonixin, clotrimazole, dexamethasone, diclofenac, duloxetine, escitalopram, fluconazole, iruxol, ketorolac, lactulose, lidocaine, lorazepam, metoclopramide, mirtazapine, nadroparin, olanzapine, omeprazole, ondansetron, paracetamol, piperacillin/tazobactam, propofol, quetiapine, rifampicin, venlafaxine and zolpidem. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 23), the subject was hospitalized for an aggravated back pain (Grade 3) secondary to the underlying disease. She was treated with IV morphine. On [redacted] (Day 27), the subject recovered from aggravated back pain. The Investigator considered back pain serious and not related to study drug.

On [redacted] (Day 309), the subject experienced worsening of back pain (Grade 3) and was hospitalized for further evaluation. She was treated with morphine, dexamethasone, pregabalin, methadone, diazepam, ibuprofen and lamotrigine. On [redacted] (Day 315), the subject recovered from back pain. The Investigator considered the event of back pain serious and not related to study drug.

On [redacted] (Day 351), tumor response assessment showed disease progression. The study drug was continued inadvertently since it was initially assessed as stable disease and a re-assessment of the tumor response on [redacted] (Day 448) confirmed disease progression. The subject was subsequently withdrawn from the study and the last dose of study drug was received on [redacted] (Day 442).

被験者番号	48021001
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	心嚢液貯留/Pericardial effusion
治験薬の投与中止に至った有害事象	心嚢液貯留/Pericardial effusion

A 36-year-old pardo female was diagnosed with high grade leiomyosarcoma in uterus on 01 Dec 2010. The last date of disease progression was 24 Jan 2013. Significant medical history included aponeurosis implant tumor resection, musculoskeletal chest pain, dyspnea, biopsy of a lesion in surgical scar, biopsy of the uterine body, hysterectomy, lung biopsy, and pulmonary metastasectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed left upper lobe lung mass. Previous anticancer therapy included docetaxel, doxorubicin, gemcitabine and ifosfamide. Prior and concomitant medications included dexamethasone, enoxaparin, gabapentin, ketoprofen, metamizole, norfloxacin, ondansetron, panadeine, phenazopyridine, ranitidine and tramadol. ECOG performance status at screening was 1.

On [redacted] (Day 1) treatment with study drug was initiated.

On [redacted] (Day 7), the subject was hospitalized for pericardial effusion (Grade 3) associated with painful respiration (Grade 3) and pain in thoracic spine (Grade 3). Chest X-ray showed pleural effusion of the 2/3 of upper left lung and chest CT scan showed pericardial effusion and pulmonary nodules. ECG was normal. She was treated with ketoprofen, tramadol, ipratropium and fenoterol and was assessed not to undergo pericardiocentesis due to her clinical instability. The study drug was withdrawn due to this event and the subject received the last dose of the study drug on [redacted] (Day 1). The subject recovered from painful respiration on [redacted] (Day 11). On [redacted] (Day 12), the pleural effusion and pericardial effusion improved to Grade 2. The subject did not recover from pericardial effusion and pain in thoracic spine. The Investigator considered pericardial effusion serious and probably related to the study drug; painful respiration and pain in thoracic spine non serious and not related to the study drug.

On [redacted] (Day 78), tumor response assessment showed disease progression. On [redacted] (Day 105,104 days after the last dose), the subject died due to pericardial effusion and secondary to disease progression.

被験者番号	48091003
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	下痢/Diarrhea

A 53-year-old white female was diagnosed with intermediate grade leiomyosarcoma in left iliac on 17 Nov 2011. The last date of disease progression was 31 Oct 2012. Significant medical history included anxiety, constipation, hemangioma, athralgia, hysterectomy, tobacco use and peripheral edema. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in left iliac muscle, gluteus minimus and medius. Previous anticancer therapy included doxorubicin, gemcitabine, ifosfamide and docetaxel. Prior and concomitant medications included bromazepam, dexamethasone, diazepam, dimenhydrinate, diphenhydramine, enemas, enoxaparin, fluconazole, furosemide, gabapentin, hyoscine, lactulose, lorazepam, mannitol, metamizole, methadone, metoclopramide, mineral oil emulsion, morphine, nystatin, omeprazole, ondansetron, pamidronic acid, passiflora incarnata, potassium, pregabalin, sodium chloride, sodium picosulfate, tenoxicam, and vitamins. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 34), the subject experienced diarrhea (Grade 1) after consuming an unspecified electrolyte drink. On [redacted] (Day 36), she was hospitalized due to increase severity of diarrhea to Grade 2. She was treated with hydration with normal saline, glucose saline potassium chloride, vitamin complex, scopolamin, metoclopramide, diphenhydramine, omeprazole, enoxaparin, metadon, lorazepam, pregabalin and dimenidrate. On [redacted] (Day 38), the subject recovered. The Investigator considered the event of diarrhea serious and not related to study drug.

On [redacted] (Day 49), tumor response assessment was initially interpreted as stable disease and study drug dosing was continued. On [redacted] (Day 70), tumor response assessment was re-evaluation which confirmed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 57).

Sponsor's opinion: The diarrhea is possibly related to study drug as this is an expected event for eribulin. Without any more likely underlying cause a causal relationship with the event cannot be excluded.

被験者番号	48111004
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	呼吸不全/Respiratory failure

A 37-year-old white male was diagnosed with high grade adipocytic pleomorphic undifferentiated sarcoma in the bones and joints in the right shoulder on 16 Mar 2011. The last date of disease progression was 18 Jan 2013. Significant medical history included ostectomy, right shoulder biopsy, and pain in extremity. At Screening tumor assessments of target/non-target lesions via CT scan showed left upper lobe lung mass, tumoral mass in right humerus, and pleural effusion . Previous anticancer therapy included docetaxel, epirubicin, gemcitabine, and ifosfamide. Prior and concomitant medications included cloperastine, dexamethasone, diphenhydramine, dorflex, filgrastim, granisetron, insulin, ketoprofen, lorazepam, metformin, metoclopramide, ranitidine, tramadol, and vertigo-vomexn. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 130), the subject experienced dyspnea (Grade 2), fatigue (Grade 2) and cough (Grade 2). He was treated with cloperastin and underwent thoracentesis on [redacted] (Day 134). Due to persistence of cough and fatigue on [redacted] (Day 135), the subject was hospitalized for respiratory failure (Grade 3). On admission, he was found to have hyperglycemia (Grade 2) and thoracic cancer pain (grade 2). He was treated with hydrocortisone, fenoterol, tramadol, ipratropium, oxygen, insulin, metformin and furosemide. He recovered from dyspnea on [redacted] (Day 135) and did not recover from fatigue, cough, respiratory failure and hyperglycemia. Tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 134). The Investigator considered respiratory failure serious and not related to the study drug; hyperglycemia non-serious and not related to the study drug but related to the use of steroids; and dyspnea, fatigue, thoracic cancer pain and cough non-serious and not related to the study drug.

On [redacted] (Day 145), the subject experienced pneumonia (Grade 2). Treatment included amoxicillin with clavulanate potassium and the subject recovered from pneumonia on [redacted] (Day 150). The Investigator considered pneumonia non-serious and not related to the study drug.

The subject died on [redacted] (Day 140, 37 days from last dose) due to respiratory failure secondary to disease progression.

被験者番号	48121004
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	単麻痺/Monoplegia

A 63-year-old Japanese female was diagnosed with high grade leiomyosarcoma in uterus on 09 Nov 2011. The last date of disease progression was 24 Oct 2012. Significant medical history included allergy to mercury, deep vein thrombosis, type 2 diabetes mellitus, dyslipidemia, hypothyroidism, and hypertension. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lower lobe lung mass, liver mass at segments II and IV, right deltoid mass, nodule along the iliac vessels and multiple disseminated bone masses. The subject received previous radiotherapy to pelvis. Previous anticancer therapy included docetaxel, epirubicin, gemcitabine, and ifosfamide. Prior and concomitant medications included atenolol, bromopride, cariax, clonazepam, colecalciferol, dexamethasone, dimenhydrinate, enemas, glucose, haloperidol, insulin, lekovit ca, levothyroxine, lisador, loperamide, metamizole, metoclopramide, morphine, nystatin, omeprazole, ondansetron, panadeine co, pravastatin, rivaroxaban, sodium glycerophosphate, and zoledronic acid. ECOG performance status at screening was 1.

On [redacted] (Day 1) treatment with study drug was initiated.

On [redacted] (Day 29), the subject experienced anemia (Grade 2), leukopenia (Grade 3), neutropenia (Grade 3) and monoplegia of the right lower limb (Grade 1) Laboratory results showed neutrophil count of 0.9 x 10^9 (NR: 1.7 – 7.9), hemoglobin of 94 g/L (NR: 110 -155) and WBC of 1.6 x 10^9/L (NR: 3.7- 11). The study drug was interrupted due to leukopenia, neutropenia and monoplegia of the right lower limb. On [redacted] (Day 35), the event of monoplegia worsened to Grade 3 and she was hospitalized. She was treated with morphine, panadeineco, metamizole, sodium glycerophosphate and enema. She recovered from from anemia on [redacted] (Day 35), from leukopenia and neutropenia on [redacted] (Day 36) and did not recover from monoplegia of the right lower limb. On [redacted] (Day 37), tumor response assessment showed spinal cord compression due to disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 22). The Investigator considered monoplegia serious and not related to the study drug but related to disease progression; and anemia, leukopenia and neutropenia non-serious and probably related to the study drug.

被験者番号	48121005
投与群	本薬群：1.4 mg/m^2 IV on Days 1 and 8, every 21 days
死亡以外の重篤な有害事象	腹痛/Abdominal pain，呼吸困難/Dyspnea

A 36-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 02 Mar 2012. The last date of disease progression was 10 Nov 2012. Significant medical history included anemia, retroperitoneal tumor excision, cholelithiasis, dyspnea, and hysterectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe lung mass, pleural effusion, left pleural mass, pleura paramediastinal and colorectal mass. Previous anticancer therapy included docetaxel, doxorubicin, gemcitabine, and ifosfamide. Prior and concomitant medications included biotene, ceftriaxone, cobaldoze, diazepam, dimenhydrinate, droperidol, duloxetine, enoxaparin, fish oil, furosemide, haloperidol, methadone, morphine, omeprazole, ondansetron, pruina, quetiapine, ranitidine and tears naturale. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 13), the subject experienced abdominal pain and was hospitalized the following day (Day 14) with dyspnea (Grade 4) and abdominal pain (Grade 3). Chest CT scan showed an increase in number and size of pulmonary lesions occupying right middle and lower lobe. Tumor response assessment showed disease progression and the subject was withdrawn from study. The last dose of the study drug was received on [redacted] (Day 8). The subject was treated with buscopan, paracetamol, hydrocortisone, metamizole, aminophylline, sodium chloride, methylprednisolone and potassium. The subject recovered from abdominal pain on [redacted] (Day 21) and was recovering from dyspnea. The Investigator considered dyspnea and abdominal pain serious and not related to the study drug.

転帰が死亡の重篤な有害事象（ダカルバジン群；3例）

被験者番号	11211026
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
転帰が死亡の重篤な有害事象	呼吸不全/Respiratory failure
死亡以外の重篤な有害事象	貧血/Anaemia，労作性呼吸困難/Dyspnoea exertional，呼吸不全/Respiratory failure
病勢進行による死亡	Yes

A 73-year-old white female was diagnosed with high grade leiomyosarcoma in right chest wall on 25 Aug 2008. The last date of disease progression was 18 Jan 2012. Significant medical history included alopecia, anemia, aortic arteriosclerosis, peripheral edema, pulmonary valve calcification, coronary artery arteriosclerosis, spinal osteoarthritis, diabetes mellitus, diastolic dysfunction, hypertension, hypertriglyceridemia, increased glycosylated hemoglobin, increased blood creatinine, cough, aortic stenosis, mitral valve calcification, mitral valve incompetence, tricuspid valve incompetence, dementia, pulmonary hypertension, malignant pleural effusion, dyspnea, pleural cavity aspiration, hysterosalpingo-oophorectomy and mass excision. At Screening, tumor assessments of target/non-target lesions via CT scan showed right pleural mass, pleural effusion and pericardial effusion. The subject received previous radiotherapy to anterior chest wall and previous anticancer therapy included docetaxel, doxorubicin and gemcitabine. Prior and concomitant medications included acetylsalicylic acid, ciprofloxacin, bisacodyl, calcium, colecalciferol, dexamethasone, diphenhydramine, docusate, enemas, enoxaparin, filgrastim, fish oil, glipizide, granisetron, heparin, lisinopril, lorazepam, macrogol, magnesium hydroxide, metformin, metoclopramide, midazolam, minerals w/vitamins, morphine, ondansetron, pantoprazole, pegfilgrastim, piperacillin/tazobactam platelets transfusion, packed red blood cells transfusion, senna alexandrina, simvastatin, and vicodin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 28) the subject experienced anemia (Grade 2) with RBC count 2.6 x 10^9/L (NR: 3.7 – 5.2), hemoglobin was 80 g/L (NR: 110-155) and hematocrit was 24% (NR: 33-47). On [redacted] (Day 29), the subject was hospitalized for anemia and worsening of exertional dyspnea (Grade 3) which started as Grade 2 on [redacted] (Day 8). CT of chest showed slight increase in the size of right pleural masses with extension to the right hilum and mediastinum with more volume loss in the right lung and a slight increase in the size of mediastinal adenopathy. Chest x-ray showed low lung volumes, enlarged heart, rounded pleural based masses in the right lung, atelectasis or infiltrated right lung base and central line tip in SVC. The subject was transfused with red blood cells and given oxygen supplementation. The study drug dose was reduced to 800 mg/m2 due to exertional dyspnea and anemia. The subject recovered from both these events. The Investigator considered exertional dyspnea serious and not related to the study drug but related to lung metastases; anemia serious and possibly related to the study drug.

On [redacted] (Day 58), the study drug was reduced to 600 mg/m2 due to thrombocytopenia which started on [redacted] (Day 15) as Grade 4 with platelet count of 15 x 10^9/L (NR: 125-375). The subject was transfused with platelets and improved. On [redacted] (Day 71), the thrombocytopenia improved to Grade 2. The Investigator considered thrombocytopenia non-serious and possibly related to the study drug.

On [redacted] (Day 59), the subject was hospitalized for respiratory failure (Grade 4) with symptoms of pyrexia (Grade1) and hypotension (Grade 3). The subject also experienced acute renal failure (Grade 1), increased blood creatinine (Grade 2), pneumonia (Grade 3), hypokalemia (Grade 1), shock (Grade 3), dehydration (Grade 3), hypocalcemia (Grade 2), malignant pleural effusion (Grade 2) and congestive cardiac failure (Grade 2). The subject was treated with oxygen, piperacillin/tazobactam potassium, sodium chloride paracetamol, vancomycin, ciprofloxacin, levofloxacin, furosemide, glyceryl trinitrate, norepinephrine, and fentanyl. On [redacted] (Day 74, 16 days after last dose), the subject died due to worsening of respiratory failure secondary to disease progression. The last dose of the study drug was received on [redacted] (Day 58). The Investigator considered respiratory failure serious and not related to the study drug but related to underlying disease progression and all other events were non-serious and not related to the study drug.

被験者番号	19081007
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
転帰が死亡の重篤な有害事象	全身健康状態低下/General physical health deterioration
死亡以外の重篤な有害事象	全身健康状態低下/General physical health deterioration, 腸閉塞/Intestinal obstruction
病勢進行による死亡	Yes

A 51-year-old male was diagnosed with intermediate grade dedifferentiated adipocytic sarcoma in retroperitoneum on 05 Sep 2011. The last date of disease progression was 03 Aug 2012. Significant medical history included abdominal pain, decreased appetite, constipation, diarrhea, inflammatory syndrome, resection of a lesion of the right thigh, mass excision, genital herpes and gastric ulcer. At Screening, tumor assessments of target/non-target lesions via CT scan showed lingular pulmonary nodules, left upper lobe lung mass, pelvic mass sarcomatosis, pulmonary nodules and abdominal masses sarcomatosis. The subject received previous radiotherapy to the right leg and previous anticancer therapy included doxorubicin, cyclophosphamide and ifosfamide. Prior and concomitant medications included amino acids w/carbohydrates, erythrocytes, esomeprazole, fluconazole, fluindione, macrogol, menadione, methylprednisolone, metoclopramide, midazolam, movicol, ondansetron, oxycodone, paracetamol, solutions for parenteral nutrition, sterculia urens, stomatologicals, tinzaparin, tramadol, valaciclovir, and zolpidem. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 10), the subject was hospitalized for sudden increase in abdominal pain and was diagnosed with intestinal obstruction (Grade 3). X-ray of plain abdomen showed several air-fluid levels on the left lateral decubitus film. The subject was treated with morphine and spasfon. On [redacted] (Day 13), the subject recovered from this event and was discharged from the hospital. The Investigator considered this event serious and not related to the study drug but related to the tumor progression.

On [redacted] (Day 17), the subject experienced a sudden increase in abdominal pain (Grade 3) with liquid stools (Grade 2). The subject was hospitalized for intestinal obstruction. Abdominal CT scan showed tumor thrombosis of portal vein, enlarged mass, signs of occlusion of the small intestine. Treatment included unspecified anti-emetics, morphine and the subject was placed on total parenteral nutrition. On [redacted] (Day 18), the subject experienced worsening of general condition and a repeat CT scan showed radiological disease progression. The subject was withdrawn from the study due to disease progression and he received the last dose of the study drug on [redacted] (Day 1). On [redacted] (Day 21, 20 days after last drug dose), the subject died due to worsening of general physical health deterioration secondary to disease progression. The Investigator considered intestinal obstruction and general health worsening serious and not related to the study drug.

被験者番号	22061002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
転帰が死亡の重篤な有害事象	心停止/Cardiac arrest
病勢進行による死亡	Yes

A 59-year-old white female was diagnosed with high grade leiomyosarcoma in right thigh on 27 Jul 2010. The last date of disease progression was 28 Dec 2012. Significant medical history included appendicectomy, inguinal hernia repair, cough, haemoptysis and musculoskeletal pain. At Screening, tumor assessments of target/non-target lesions via CT scan showed right middle lobe lung mass and lung mass: bilaterally lung parenchyma. The subject received previous radiotherapy to right thigh and previous anticancer therapy included gemcitabine, doxorubicin, and ifosfamide. Prior and concomitant medications included codeine, fentanyl, levosulpiride, omeprazole, ondansetron, oxycodone, and tranexamic acid. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 42), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 22). On [redacted] (Day 43), her ECOG performance status was 4. On [redacted] (Day 52, 30 days after last dose), the subject died due to cardiac arrest secondary to disease progression. The Investigator considered this event serious and not related to the study drug.

死亡以外のその他の重篤な有害事象（ダカルバジン群；68例）

被験者番号	11011002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	胸水/Pleural effusion

A 59-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 01 Jun 2011. The last date of disease progression was 30 Oct 2012. Significant medical history included arthritis, hyperlipidemia, hypertension, ostectomy, seasonal allergies, female sterilisation, sleep apnea syndrome, type 2 diabetes mellitus, and total abdominal hysterectomy with bilateral salpingo-oopherectomy. At Screening, tumor assessments of target/non-target lesions via spiral CT scan showed left upper lobe and righ lower lobe lung mass and multiple bilateral pulmonary nodules. Previous anticancer therapy included investigational drug (palifosfamide), doxorubicin, gemcitabine, docetaxel and trabectedin. Prior and concomitant medications included alprazolam, ascorbic acid, cyanocobalamin, docusate, doxycycline, diphenhydramine/paracetamol, fluoxetine, glimepiride, insulin, lidocaine, lisinopril, meclozine, oxycodone, prochlorperazine and metformin/sitagliptin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 13) the subject was hospitalized for pleural effusion of unknown etiology (Grade 3). As per hospital report, a chest x-ray showed increased right pleural effusion partially obscuring metastatic disease in the right lower lobe. She was treated with doxycycline and lidocaine. Pleurodesis and pigtail catheter thoracentesis were performed and the subject recovered on [redacted] (Day 20). The Investigator considered pleural effusion serious and not related to the study drug.

On [redacted] (Day 43), tumor response assessments showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 22).

被験者番号	11031006
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	白血球減少症/Leukopenia

A 66-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 12 Mar 2009. The last date of disease progression was 01 Aug 2012. Significant medical history included anemia, bone pain, hypercholesterolemia, dyspnea, bilateral omentectomy, bilateral salpingo-oophorectomy, cataract surgery, diabetes mellitus, excision of tumor implants, total abdominal hysterectomy, cholelithiasis, hiatal hernia, hyperuricemia, diarrhea, vomiting, nausea, resection of recurrent pelvic tumor, sinus tachycardia, small bowel resection, small bowel resection with re-anastomosis. At Screening, tumor assessments of target/non-target lesions via CT scan showed lower abdominal mass, dominant pelvic mass, smaller pelvic mass, pericentric lesion in the left mid abdomen and left lower pelvic mass. Previous anticancer therapy included doxorubicin, gemcitabine, antineoplastic agents (TH-302) docetaxel and trabectedin. Prior and concomitant medications included allopurinol, alpha-d-galactosidase, cyanocobalamin, ibuprofen, iron, lorazepam, lovastatin, magnesium, metformin, ondansetron, prochlorperazine, red blood cells and sodium chloride. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 42), the subject experienced leukopenia (Grade 3). Laboratory results showed WBC count 1.8 x 10^9/L (NR: 3.7-11). She recovered on [redacted] (Day 77) and her repeat WBC count was 3.4 x 10^9/L. The Investigator considered leukopenia serious (important medical event) and probably related to the study drug.

On [redacted] (Day 98), the subject experienced neutropenia (Grade 3). Laboratory results showed neutrophil count of 0.84 x 10^9/L (NR: 1.7 – 7.9). She recovered on [redacted] (Day 112) and the study drug dose was reduced to 800 mg/m2 on the same day. The Investigator considered neutropenia non-serious and probably related to the study drug.

On [redacted] (Day 461), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 434).

被験者番号	11031008
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	小腸閉塞/Small intestinal obstruction
病勢進行による死亡	不明

A 65-year-old white male was diagnosed with intermediate grade myxoid adipocytic tumor in retroperitoneum on 12 Dec 2006. The last date of disease progression was 10 Jul 2012. Significant medical history included appendicectomy, peripheral sensory neuropathy, hemorrhoids, left radical nephrectomy, lymphoedema, tendon operation, right knee surgery, abdominal hernia repair, abdominal pain, cellulitis, allergies to iodinated radio contrast dyes and penicillin, ureteral stent insertion, sarcoma excision, small intestinal resection, left hyrdronephrosis, thoracic cavity drainage, post herpetic neuralgia, resection of multicentric carcinoid tumor and herpes zoster. At Screening, tumor assessments of target/non-target lesions via CT scan showed left abdominal mass, left pelvic mass and left anterior pelvicmass. The subject received previous radiotherapy to recurrent retroperitoneal liposarcoma. Previous anticancer therapy included th302, docetaxel, doxorubicin, gemcitabine, and pazopanib. Prior and concomitant medications included calcium carbonate, fentanyl, gabapentin, lomotil, ondansetron, oxycodone, sodium chloride solutions and prochlorperazine. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 85), the subject was hospitalized for small intestinal obstruction (Grade 3) with symptoms of chills (Grade 1), nausea (Grade 2), vomiting (Grade 2), abdominal pain (Grade 1), reduced bowel movements (Grade 1) and vestibular disorder (Grade 1). CT scan of abdomen showed a left lower quadrant small bowel obstruction secondary to tumor. On the same day, tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 78). The subject underwent intermittent nasogastric tube suction and was treated with zofran and dilaudid. The subject wished for DNR/DNI and was placed in comfort measures. The subject did not recover from this event. On [redacted] (Day 98, 20 days after last dose), the subject died due to an unknown cause and no autopsy was done. The Investigator considered small intestinal obstruction serious and not related to the study drug, but related to underlying tumor.

被験者番号	11041005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腹部膨満/Abdominal distension

A 42-year-old hispanic male was diagnosed with high grade myxoid liposarcoma in the retroperitoneum on 14 Apr 2010. The last date of disease progression was 07 Nov 2011. Significant medical history included abdominal discomfort, abdominal tumor resection, early satiety, elevated alkaline phosphatase, gastroesphageal reflux disease, neutropenia, intermittent abdominal pain, intermittent constipation, intermittent diarrhea, intermittent nausea, left thigh tumor excision, arthralgia, cancer pain, paraesthesia, vomiting and upper respiratory tract infection. At Screening, tumor assessments of target/non-target lesions via spiral CT scan showed liver, abdominal and pelvic mass. Previous anticancer therapy included doxorubicin, gemcitabine, docetaxel and trabectedin. Prior and concomitant medications included human albumin, antacids with antiflatulents, azithromycin, bisacodyl, bumetanide, ciprofloxacin, esomeprazole, fentanyl, furosemide, granisetron, hydromorphone, influenza vaccine, lorazepam, macrogol, metoclopramide, morphine, omeprazole, ondansetron, pantoprazole, codeine/paracetamol, prochlorperazine, senna alexandrina, sodium chloride and zolpidem. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 43), the subject was hospitalized for abdominal distension (Grade 2), generalized edema (Grade 2) and scrotal edema (Grade 1). Laboratory results showed AST 26 IU/L (NR: 10-43); ALT of 12 IU/L (NR: 10-40); alkaline phosphatase of 228 IU/L (NR: 43-115) and albumin of 34g/L (NR: 35-55). He underwent abdominal ultrasound in anticipation for paracentesis but it revealed the abdomen was filled with solid tumor and only a tiny amount of fluid was in the abdomen. He was treated with furosemide and bumetanide and the events were ongoing. On the same day, the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 23). The Investigator considered abdominal distention serious and not related to the study drug; generalized edema and scrotal edema non-serious and not related to the study drug.

被験者番号	11061002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	肺炎/Pneumonia

A 50-year-old white male was diagnosed with high grade pleomorphic liposarcoma in right thigh on 03 May 2011. The last date of disease progression was 25 Apr 2012. Medical history included degenerative disc disease, hypothyroidism, intermittent constipation, intermittent hemoptysis, lymphedema, myalgia, neuralgia, monoplegia, productive cough, nasal congestion, dyspnea, diarrhea, intermittent constipation, sleep apnea syndrome and left anterior medial thigh sarcoma excision. At Screening, tumor assessments of target/non-target lesions via CT scan showed right upper lobe and lower lobe lung masses, left lingular lobe lung mass, left lower lobe lung mass and left pleura lung mass. The subject received previous radiotherapy to left inner thigh. Previous anticancer therapy included doxorubicin, ifosfamide, palifosfamide-tris/placebo and trabectedin. Prior and concomitant medications included clonazepam, dexamethasone, duloxetine, levothyroxine, lorazepam, metoprolol, morphine, ondansetron, oxycodone, pegfilgrastim, pentoxifylline, pramipexole, pregabalin, prochlorperazine and red blood cells. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 42), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 22).

On [redacted] (Day 46), the subject was hospitalized for pneumonia (Grade 3) and was treated with levofloxacin, vancomycin, cefepime and fluconazole. He recovered from pneumonia on [redacted] (Day 52). The Investigator considered pneumonia serious and possibly related to the study drug.

被験者番号	11091001
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	低血圧/Hypotension

A 63-year-old white female was diagnosed with high grade leiomyosarcoma in retroperitoneum on 23 Jul 2010. The last date of disease progression was 22 Oct 2011. Significant medical history included anemia, asthma, dyslipidemia, elevated alkaline phosphatase, spinal laminectomy, hypoalbuminemia, hypokalemia, hypomagnesemia, diarrhea, hypertension, nausea, tumor pain, paroxysmal atrial tachycardia, peripheral vascular disease, resection of primary tumor in pelvis, cystopexy and total abdominal hysterectomy with bilateral salpingo-oopherectomy. At Screening, tumor assessments of target/non-target lesions via spiral CT scan showed right upper lobe lung mass, left lateral lobe liver mass, right lower lobe liver mass, left kidney mass, multiple lung lesions over several lobes and multiple liver lesions across all segments. The subject received previous radiotherapy to the pelvic bed, single lesion in rib, and left upper lobe lung mass. Previous anticancer therapy included docetaxel, gemcitabine, doxorubicin, and vinorelbine. Prior and concomitant medications included acetylsalicylic acid, clopidogrel, diphenhydramine, dronabinol, fluoxetine, lomotil, lorazepam, magnesium oxide, magnesium sulfate, megestrol, methylprednisolone, morphine, nitrofurantoin, omeprazole, oxycodone/acetaminophen, papaver somniferum, potassium, prochlorperazine, sotalol and zestoretic. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 37), the subject presented to radiology for restaging scans and had a near syncopal episode. She experienced hypotension (Grade 3) with blood pressure of 72/56 mm Hg (NR: 120/80 – 140/90). She was treated with sodium chloride and recovered. The tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 22). The Investigator considered hypotension serious (important medical event) and possibly related to the study drug.

被験者番号	11101001
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	血小板減少症/Thrombocytopenia

A 69-year-old white male was diagnosed with intermediate grade dedifferentiated liposarcoma in retroperitoneum on 10 Jan 1997. The last date of disease progression was 14 Sep 2011. Significant medical history included coloproctostomy, venous operation, adhesiolysis, herpes zoster, central venous catheterisation, colectomy, myocardial infarction, neurolysis, pain in extremity, peptic ulcer disease, duodenal operation, sarcoma excisions, renal mass excision, tumour excision, adrenalectomy, coronary arterial stent insertion, diabetes mellitus, pancreatico splenectomy, duodenum ulcer, dysaesthesia, gout, hyperlipidemia, hypertension, gastrectomy, large intestine anastomosis and ultrasound-guided prostate needle biopsy. At Screening, tumor assessments of target/non-target lesions via CT scan showed left para-aortic soft tissue masses and multiple retroperitoneal soft tissue masses. The subject received previous radiotherapy to right lateral border of vena cava spine and down to the psoas muscle, and the entire peritoneal defect with exposed iliacus and psoas muscles, nerves, the artery and the vein. Previous anticancer therapy included doxorubicin, trabectedin, investigational drug (R7112) and troglitazone. Prior and concomitant medications included acetylsalicylic acid, filgrastim, glimepiride, insulin glargine, lisinopril, nystatin, ondansetron, prochlorperazine and simvastatin. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 8), the subject experienced thrombocytopenia (Grade 1), which increased its severity to Grade 3 on [redacted] (Day 15) with platelet count of 51 x 10^9/L (NR: 125-375). On [redacted] (Day 20), the thrombocytopenia worsened to Grade 4 with platelet count of 14 x 10^9/L and decreased white blood cell count (Grade 2) with WBC count of 2.7 x 10^9/L (NR: 3.7 – 11) and decreased neutrophil count (Grade 1) with absolute neutrophil counts (ANC) 1.48 x 10^9/L (NR: 1.7 – 7.9). The study drug was interrupted due to these events. The subject was transfused with platelets and treated with filgrastim. The subject's thrombocytopenia improved to Grade 2 on [redacted] (Day 22) with platelet count of 64 x 10^9/L (NR: 125-375). The events of decreased white blood cell count and decreased neutrophil count worsened to Grade 3 on [redacted] (Day 22) with WBC count of 1.7 x 10^9/L and ANC of 0.8 x 10^9/L respectively. His thrombocytopenia worsened again to Grade 3 on [redacted] (Day 27), and then improved to Grade 2 on [redacted] (Day 29). The subject recovered from decreased white blood cell count and decreased neutrophil count on [redacted] (Day 34) and from thrombocytopenia on [redacted] (Day 43). The Investigator considered thrombocytopenia serious (important medical event) and probably related to the study drug; decreased white blood cell count and decreased neutrophil count non-serious and probably related to the study drug.

On [redacted] (Day 29), the subject withdrew from the study by choice and received the last dose of the study drug on [redacted] (Day 1).

被験者番号	11141007
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anaemia，憩室/Diverticulum，胃腸出血/Gastrointestinal haemorrhage，血小板減少症/Thrombocytopenia

A 56-year-old hispanic female was diagnosed with high grade leiomyosarcoma in uterus on 21 Jul 2010. The last date of disease progression was 05 Dec 2012. Significant medical history included abdominal pain, abdominoplasty, cholecystectomy, cystoscopy with fulguration for gross hematuria, bilateral lower extremitiesn edema, exploratory laparotomy and radical resection of pelvic sarcoma, gastrooesophageal reflux disease, Grave's disease, hematuria, haitus hernia, anemia, hydronephrosis, hypercholesterolemia, left thoracotomy with medial basilar segmentectomy, rhabdomyolysis, pollakiuria, diverticulosis and uterine fibroids. At Screening, tumor assessments of target/non-target lesions via CT scan showed right pelvic lesion. Previous anticancer therapy included doxorubicin, ifosfamide, pazopanib, investigational drug, gemcitabine, docetaxel and trabectedin. Prior and Concomitant medications included acrivastine, colecalciferol, cyanocobalamin, folic acid, furosemide, hydrocodone, lekovit ca, metoclopramide, omeprazole, ondansetron, potassium, prochlorperazine, senokot-s, thiamazole, tramadol, vicodin and vitamins. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 80), the subject was hospitalized for anemia (Grade 3), diverticulosis (Grade 3), thrombocytopenia (Grade 4) and gastrointestinal hemorrhage (Grade 3). Laboratory results showed hemoglobin of 69 g/L (NR: 110 - 155), hematocrit of 21.4% (NR: 33 – 47) and platelets of 21 x 10^9/L (NR: 150-400). The subject was transfused with platelets and packed cells and she recovered on [redacted] (Day 86) from all these events. The Investigator considered anemia and thrombocytopenia serious and probably related to the study drug; diverticulosis serious and not related to the study drug and gastrointestinal hemorrhage serious and possibly related to the study drug.

On [redacted] (Day 134), the subject was hospitalized for gastrointestinal hemorrhage (Grade 3) and thrombocytopenia (Grade 3) with hemoglobin of 87 g/L and platelets of 38 x 10^9/L. The subject was transfused with platelets and packed red cells. The subject recovered from gastrointestinal hemorrhage on [redacted] (Day 137) and from thrombocytopenia on [redacted] (Day 142). On [redacted] (Day 148), the study drug dose was reduced to 600 mg/m^2 due to thrombocytopenia. The Investigator considered gastrointestinal hemorrhage serious and possibly related to the study drug and thrombocytopenia serious (important medical event) and probably related to the study drug.

On [redacted] (Day 169), the study drug dose was increased to 800 mg/m^2 by the Investigator. On [redacted] (Day 184), the subject was hospitalized for gastrointestinal hemorrhage (Grade 3) secondary to tumor invasion with hemoglobin of 73 g/L and hematocrit of 22.6%. The subject was transfused with packed cells and recovered on [redacted] (Day 194). The Investigator considered this event serious and not related to the study drug.

On [redacted] (Day 197), the subject was withdrawn from the study by the Investigator due to drug intolerance. The subject received the last dose of the study drug on [redacted] (Day 169).

被験者番号	11141010
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	発熱性好中球減少症/Febrile neutropenia，血小板減少症/Thrombocytopenia

A 46-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 02 Feb 2009. The last date of disease progression was 27 Mar 2013. Significant medical history included elevated alanine aminotransferase, elevated aspartate aminotransferase, elevated alkaline phosphatase, hepatic steatosis, paratubal cystectomy, arthralgia, pain in extremity, and hysterectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lateral liver mass and right pelvic mass. Previous anticancer therapy included doxorubicin, ifosfamide, gemcitabine, docetaxel and trabectedin. Prior and concomitant medications included celecoxib, cetirizine, coloxyl with senna, fentanyl, hydromorphone, methadone, ondansetron, prochlorperazine, promethazine, tramadol, hydrocodone/acetaminophen, and vitamins. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15), the subject was hospitalized for thrombocytopenia (Grade 4), and febrile neutropenia (Grade 3) with platelet count of 7 x10^9/L (NR: 125-375), absolute neutrophil count of 0.9 x10^9/L (NR: 1.7-7.9), and WBC count of 2.8 x 10^9/L (NR: 3.7 – 11). The subject was transfused with platelets, and treated with cefepime, levofloxacin, filgrastim, and ciprofloxacin. On [redacted] (Day 19), febrile neutropenia worsened to Grade 4 with absolute neutrophil count 0.1 x 10^9/L. The subject recovered from febrile neutropenia on [redacted] (Day 23) and the thrombocytopenia improved to Grade 3. The subject recovered from thrombocytopenia on [redacted] (Day 27). The Investigator considered thrombocytopenia and febrile neutropenia serious and probably related to the study drug. On [redacted] (Day 36), the study drug dose was reduced to 600mg/m^2 due to thrombocytopenia.

On [redacted] (Day 56), the study drug dose was increased to 750 mg/m^2 by the Investigator. On [redacted] (Day 70), the subject experienced thrombocytopenia (Grade 4) and on [redacted] (Day 75), the thrombocytopenia decreased in severity to Grade 3 and recovered on [redacted] (Day 78). The Investigator considered thrombocytopenia non-serious and probably related to the study drug.

On [redacted] (Day 83), the subject was withdrawn from the study by the Investigator due to drug intolerance. The subject received the last dose of the study drug on [redacted] (Day 57).

被験者番号	11151001
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	呼吸困難/Dyspnea, 悪性胸水/Malignant pleural effusion

A 35-year-old white male was diagnosed with intermediate grade adipocytic myxoid mass in left thigh on 17 Dec 2009. The last date of disease progression was 06 Jan 2012. Medical history included anxiety, hyperlipidema, alopecia, hypoaesthesia and peripheral sensory neuropathy. At Screening, tumor assessments of target/non-target lesions via CT scan showed mediastinal index lymphadenopathy, pleural based soft tissue density in right hemithorax, left lingular lobe lung lesion and bilateral lung micronodules. The subject received previous radiotherapy to soft tissue extremity and left shoulder girdle lesion. Previous anticancer therapy included doxorubicin, ifosfamide, gemcitabine, and docetaxel. Prior and concomitant medications included alprazolam, calcium carbonate with vitamin D, cyclobenzaprine, enoxaparin, fish oil, fluconazole, ibuprofen, influenza vaccine, lidocaine, morphine, promethazine, sertraline, sodium chloride, vicodin and vitamins. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 36), the subject was hospitalized for dyspnea (Grade 2), non-cardiac chest pain (Grade 2) and malignant pleural effusion (Grade 2). He underwent thoracocentesis and was treated with ibuprofen, cyclobenzaprine, vicodin, morphine and lidocaine. He recovered from malignant pleural effusion and non-cardiac chest pain on [redacted] (Day 43) and from dyspnea on [redacted] (Day 46). The Investigator considered malignant pleural effusion and dyspnea serious and not related to the study drug; non-cardiac chest pain non-serious and not related to the study drug but related to disease progression.

On [redacted] (Day 43), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received last dose of the study drug on [redacted] (Day 22).

被験者番号	11191005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	肺炎/Pneumonia，腹水/Ascites[注)]，呼吸困難/Dyspnea[注)]

注）腹水及び呼吸困難は，重篤な有害事象として集計されていない。

A 75-year-old white male was diagnosed with high grade leiomyosarcoma in lung and bronchus on 28 Apr 2009. The last date of disease progression was 29 Dec 2011. Medical history included anemia, cardiac murmur, asthma, bilateral leg pain, bilateral pulmonary angiogram, chronic back pain, diabetes mellitus, endarterectomy, endovascular biopsy, exertional dyspnoea, palmar-plantar erythrodysaesthesia syndrome, hypertension, cardiac catheterisation , low platelet count, lower extremity edema, hyperkeratosis, cough, skin exfoliation, neuropathic pain bilateral feet, palpatations, prostectomy, vascular pseudoaneurysm, pulmonary valvulplasty, pulmonary hypertension, right iliofermoral angiogram, dyspnea, syncope, and tachycardia. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lower lobe lung mass, left adrenal gland mass and splenic mass. The subject received previous radiotherapy to chest wall in association with axillary node radiation, left upper lobe lung massand ribs 3, 4, 5 and some residual paravertebral mass. Previous anticancer therapy included doxorubicin, gemcitabine, docetaxel and sorafenib. Prior and concomitant medications included acetylsalicylic acid, amoxicillin, aprepitant, augmentin, bactrim, benazepril, benzonatate, bismuth, dexamethasone, docusate, furosemide, heparin, hydromorphone, influenza vaccine, insulin glargine, levofloxacin, magnesium sulfate, metoclopramide, morphine, nystatin, ondansetron, pantoprazole, pneumococcal vaccine, potassium, procet, prochlorperazine, red blood cells and warfarin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 160), the subject experienced worsening cough (Grade 2). The subject was treated with bactrim, levofloxacin and augmentin. He did not recover. On [redacted] (Day 235), the study drug dose was reduced to 850 mg/m^2 due to this event. The Investigator considered cough non-serious and not related to the study drug.

On [redacted] (Day 255), the subject was hospitalized for pneumonia (Grade 3). He was treated with levofloxacin and recovered on [redacted] (Day 256). The Investigator considered pneumonia serious and possibly related to the study drug. The study drug dose was not changed.

On [redacted] (Day 307), the subject was hospitalized for ascites (Grade 2). On [redacted] (Day 313), the subject experienced dyspnea (Grade 3) along with pericardial thickening (Grade1) and jugular vein thrombosis (Grade 1). He underwent echocardiogram and paracentesis and one liter of fluid was drained. He was treated with lasix, heparin, warfarin and hydromorphone. He recovered from ascites on [redacted] (Day 331). On the same day, the subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 274). The subject did not recover from shortness of breath, jugular vein thrombosis and pericardial thickening. The Investigator considered ascites and dyspnea serious and not related to the study drug but related to the disease; pericardial thickening and jugular vein thrombosis non-serious and not related to the study drug.

被験者番号	11191006
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	頭蓋内腫瘍出血/Intracranial tumour haemorrhage

A 64-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 19 Nov 2010. The last date of disease progression was 30 Jan 2012. Significant medical history included hypothyroidism, urinary tract infection, arthralgia, intermittent hip pain, arthralgia, nausea, muscular weakness and peripheral sensory neuropathy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right upper and lower lobe lung mass, left lateral lobe liver mass, cervical vertebral mass and T9 lytic lesion. Previous anticancer therapy included gemcitabine, docetaxel, bevacizumab and doxorubicin. Prior and concomitant medications included alprazolam, bactrim, bisacodyl, ciprofloxacin, clonazepam, dexamethasone, diphenhydramine, famotidine, levetiracetam, levothyroxine, liothyronine, lorazepam, ondansetron, phenytoin, piperacillin/tazobactam, prochlorperazine, quetiapine, temazepam, vancomycin and zolpidem. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 35), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 21).

On [redacted] (Day 36), the subject was hospitalized for right occipital lobe hemorrhagic tumor mass (Grade 3). On [redacted] (Day 38), the subject experienced pyrexia (Grade 2). The subject underwent MRI of brain which revealed a right occipital hemorrhaging mass measuring 4.3 cm with surrounding edema. The subject was treated with vancomycin, quetiapine piperacillin/tazobactam and levitracetam. The subject recovered on [redacted] (Day 41). The Investigator considered right occipital lobe hemorrhagic tumor mass serious and not related to the study drug; pyrexia non-serious and not related to the study drug.

被験者番号	11211005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	しゃっくり/Hiccups
病勢進行による死亡	Yes

A 57-year-old white male was diagnosed with high grade leiomyosarcoma in retroperitoneum on 15 Mar 2010. The last date of disease progression was 16 Mar 2011. Significant medical history included abdominal pain, alopecia, gastrointestinal motility disorder, anaemia, decreased appetite, asthenia, coronary arterial stent insertion, vena cava thrombosis, deep venous thrombosis left leg, gastrooesophageal reflux disease, hypercholesterolaemia, hypertension, hypothyroidism, non-cardiac chest pain, peripheral edema, leukocytosis, cerebrovascular accident and dyspnea. At Screening, tumor assessments of target/non-target lesions via CT scan showed peritoneal/omental mass, right lower lobe liver mass, pancreatic mass, rectal mass, right upper lobe and right middle lobe lung masses, and kidney mass. Previous anticancer therapy included docetaxel, doxorubicin, gemcitabine and th-cr-302 (investigational drug). Prior and concomitant medications included atorvastatin, dalteparin, dexamethasone, diphenhydramine, docusate, ezetimibe, glyceryl trinitrate, hydromorphone, levothyroxine, lisinopril, lorazepam, macrogol, magnesium, magnesium hydroxide, morphine, nicotinic acid, omeprazole, ondansetron, paracetamol, prochlorperazine, red blood cells, vicodin, and vitamins. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 37), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 29).

On [redacted] (Day 47), the subject was hospitalized for hiccups (Grade 3) and the subject was treated with baclofen and prochlorperazine. On [redacted] (Day 51), the subject recovered from this event. On [redacted] (Day 52, 23 days after last dose), the subject died due to disease progression. The Investigator considered hiccups serious and not related to the study drug but related to diaphragmatic irritation.

被験者番号	11211028
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腸閉塞/Intestinal obstruction，小腸閉塞/Small intestinal obstruction

A 59-year-old white female was diagnosed with high grade leiomyosarcoma in retroperitoneum on 04 Jun 2010. The last date of disease progression was 17 Mar 2012. Significant medical history included abdominal pain, anemia, atherosclerotic changes of thoracic aorta, bilateral lower extremity edema, closure of small bowel defect, large intestine anastomosis, colostomy, CT guided placement of drainage catheter in left lower abdomen for fluid collection, spinal osteoarthritis, gastrointestinal dilation procedure, en bloc colectomy, colostomy, intestinal anastomosis, intestinal adhesion lysis, hepatic steatosis, , adrenal mass, jejunectomy, nephrostomy, ureteral stent insertion, mitral valve incompetence, incision site complication, bacterial pyelonephritis, radical resection of retroperitoneal mass, resection of descending colon with en bloc mass, resection of phylloides tumor, urostomy, resection of right upper quadrant mass with enbloc colon and small bowel mass, small bowel mesenteric mass biopsy and gastrointestinal stoma complication. At Screening, tumor assessments of target/non-target lesions via CT scan showed peritoneal mass in midline inferior abdomen, left retroperitoneal mass, left lateral inferior abdominal wall mass, midline abdomen mass, left gerotia's fascia mass, left lower quadrant para-midline mass and left peri-gastric mass. The subject received previous radiotherapy to abdominal and pelvic tumor bed. Previous anticancer therapy included gemcitabine, docetaxel and doxorubicin. Prior and concomitant medications included alprazolam, dexamethasone, enoxaparin, escitalopram, fentanyl, filgrastim, granisetron, heparin, hydromorphone, lorazepam, magnesium sulfate, metoclopramide, montelukast, ondansetron, pantoprazole, pegfilgrastim, potassium chloride, probiotics, prochlorperazine, sertraline, sodium chloride, trazodone and zoledronic acid. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 83), the subject was hospitalized for small intestine obstruction (Grade 2). She underwent CT scan of the abdomen and nasogastric tube insertion. She was treated with morphine, granisetron and normal saline and recovered on [redacted] (Day 85). The Investigator considered this event serious and not related to the study drug.

On [redacted] (Day 523), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 510).

On [redacted] (Day 527), the subject experienced abdominal pain (Grade 2), nausea (Grade 1) and vomiting (Grade 1). On [redacted] (Day 528), the subject was hospitalized for intestinal obstruction (Grade 3) which was related to scarring from previous surgery and dehydration (Grade 2). She was treated with normal saline, ondansetron, fentanyl patch, metoclopramide, hydromorphone, metoclopramide, and prochlorperazine. Abdominal X-ray showed resolution of her small bowel obstruction and was confirmed by gastrografin study. She recovered on [redacted] (Day 532) from all these events. The Investigator considered intestinal obstruction serious and not related to the study drug; and nausea, vomiting, dehydration and abdominal pain non-serious and not related to the study drug.

被験者番号	11211030
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	好中球減少症/Neutropenia，血小板減少症/Thrombocytopenia
治験薬の投与中止に至った有害事象	骨髄異形成症候群/Myelodysplastic syndrome

A 48-year-old white female was diagnosed with high grade leiomyosarcoma in the retroperitoneum on 15 Sep 2004. The last date of disease progression was 13 Mar 2012. Significant medical history included ascites, renal atrophy, bilateral kidney cyst, biopsy of benign breast mass, bradycardia, chronic renal insufficiency, CT guided fine needle aspirate and biopsy of right lower lobe lung mass, decreased joint range motion, cancer surgery, hypercholesterolemia, hypertriglyceridemia, increased alkaline phosphatase, increased alanine aminotransferase increased, increased aspartate aminotransferase, increased creatinine, insomnia, intermittent cough, intermittent dizziness, dyspnea, musculoskeletal pain, ovarian vein thrombosis, benign neoplasm of thyroid gland, hepatic cyst, inferior vena caval occlusion, peripheral sensory neuropathy, prolonged international normalized ratio, venous repair and thrombocytopenia. At Screening, tumor assessments of target/non-target lesions via CT scan showed left para-aortic lymphadenopathy, antero-superior mid dome liver mass, subcapsular left lobe liver mass, right peri-aortic mass, left abdominal and pelvic adenopathy, multiple pleural based nodules and right dome of the liver mass. The subject received previous radiotherapy to inferior vena cava. Previous anticancer therapy included gemcitabine, docetaxel, doxorubicin and ifosfamide. Prior and concomitant medications included darbepoetin alfa, dexamethasone, diphenhydramine, docusate, hydrocortisone, hydromorphone, iron, lactulose, lansoprazole, lorazepam, morphine, ondansetron, palonosetron, paracetamol, prochlorperazine, red blood cells, vicodin and vitamins. ECOG performance status at screening was 1.On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15), the subject was hospitalized for thrombocytopenia (Grade 4) and neutropenia (Grade 3). Laboratory results showed platelet count of 96 x10^9/L (NR: 125-375) and neutrophil count of 0.9 x 10^9/L (NR: 1.7 – 7.9). On [redacted] (Day 22) the neutropenia worsened to Grade 4 with neutrophil count of 0.2 x 10^9/L. The subject was transfused with platelets and treated with filgrastim and she recovered from thrombocytopenia on [redacted] (Day 33) and from neutropenia on [redacted] (Day 49). The Investigator considered thrombocytopenia and neutropenia serious and probably related to the study drug. The study drug dose was not changed due to these events.

On [redacted] (Day 29) the subject underwent bone marrow biopsy which showed hypocellular bone marrow with marked myeloid predominance and mild dysgranulopoiesis and she was diagnosed with myelodysplastic syndrome (Grade 2). The subject was withdrawn from the study due myelodysplastic syndrome. The study drug was withdrawn from the study and the subject received the last dose of the study drug on [redacted] (Day 1). The subject did not recover from this event. The Investigator considered myelodysplastic syndrome non-serious and not related to the study drug.

被験者番号	11221004
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腹痛/Abdominal pain, 汎血球減少症/Pancytopenia

A 52-year-old white female was diagnosed with high grade dedifferentiated adipocytic sarcoma in retroperitoneum on 2008. The last date of disease progression was 19 Sep 2012. Significant medical history included abdominal pain, delirium, exploratory laparotomy, extra systoles, left abdominal pain, gastrointestinal neoplasm, nephrectomy, hepatectomy, renal failure, resection of intra-abdominal tumor, cytoreductive surgery, thrombocytopenia, herpes zoster, radiation associated hemorrhage, removal of adhesions, fibroid tumors and pelvic cysts. At Screening, tumor assessments of target/non-target lesions via CT scan showed retroperitoneal mass. The subject received previous radiotherapy to the bowel. Previous anticancer therapy included doxorubicin, gemcitabine, paclitaxel and trabectedin. Prior and concomitant medications included ascorbic acid, calcium D3, ceftazidime, diphenhydramine, docusate, eletriptan, estazolam, fexofenadine, folic acid w/pyridoxine hydrochloride, gabapentin, hydromorphone, hyoscyamine, ibuprofen, lorazepam, macrogol, metoclopramide, morphine, omeprazole, ondansetron, oxycodone, paracetamol, polycarbophil, potassium, prochlorperazine, senna alexandrina, simeticone, vancomycin and vitamins. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 14), the subject was hospitalized for worsening abdominal pain (Grade 3) and pancytopenia (Grade 3) with WBC count of 0.7 x 10^9/L (NR: 3.7 - 11), RBC count of 2.31 x10^9/L(NR: 3.7 - 5.2), platelet count of 4 x 10^9/L (NR:125-375) and hemoglobin of 74 g/L (NR:110-155). On [redacted] (Day 15), the subject experienced port-a-catheter infection (Grade 2) and petechiae on lower extremities (Grade 1). She was treated with levofloxacin, morphine, vicodin, filgrastim, and received blood transfusion and platelets transfusion. The subject's port-a-cath was removed and she recovered from the infection on [redacted] (Day 16). On [redacted] (Day 16), the subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 1). On [redacted] (Day 17), she recovered from worsening abdominal pain, pancytopenia and nausea. She did not recover from petechiea. The Investigator considered abdominal pain serious and not related to the study drug; pancytopenia serious and probably related to the study drug; nausea non-serious and probably related to the study drug and port-a-cath infection and petechiae non-serious and not related to the study drug.

被験者番号	11221007
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	平滑筋肉腫/Leiomyosarcoma

A 40-year-old white female was diagnosed with intermediate grade leiomyosarcoma in uterus on Mar 2009. The last date of disease progression was 25 Apr 2013. Significant medical history included cervicectomy, insomnia, iron deficiency anemia, hysterectomy, leukopenia, nausea, vomiting, neutropenia, cancer surgery, rheumatoid arthritis, ulcerative colitis and anemia. At Screening, tumor assessments of target/non-target lesions via CT scan showed lung mass, right perihilar lung mass, right paracardiac mass and right lower lobe lung nodule. Previous anticancer therapy included doxorubicin, gemcitabine, docetaxel, bevacizumab, paclitaxel, and trabectedin. Prior and concomitant medications included blood and related products, cetirizine, dexamethasone, diclofenac, diphenhydramine, doxylamine, fentanyl, folic acid, granisetron, hydromorphone, lorazepam, macrogol, methocarbamol, methotrexate, metoprolol, norepinephrine, oxycodone, pegfilgrastim, prochlorperazine and sulfasalazine. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 101), the subject was withdrawn from the study since the treating physician considered surgery as an alternative option. The last dose of the study drug was received on [redacted] (Day 84).

On [redacted] (Day 105) the subject was hospitalized for planned surgery for leiomyosarcoma (Grade 3) in proximity to the diaphragm. Following surgery she was transfused with red blood cells. Chest x-ray was negative for pleural effusion and she was started on metoprolol. The following chest X-ray showed pneumothorax due to air leak from chest tube and she was treated with robaxin for muscle spasm at chest tube site. She recovered on the same day. The Investigator considered leiomyosarcoma serious and not related to the study drug.

被験者番号	11231001
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	心房細動/Atrial fibrillation

A 67-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 19 Nov 2008. The last date of disease progression was 03 Oct 2011. Medical history included drug hypersensitivity to codeine, ketorolac and indomethacin, bilateral salpingo-oophorectomy, bone disorder, hypertension, osteopenia, osteoporosis, palpitations, tachycardia, total abdominal hysterectomy, atrial fibrillation, intervertebral disc degeneration and spinal fracture. At Screening, tumor assessments of target/non-target lesions via CT scan showed right pelvis lesion, liver mass near portal vein bifurcation and right lobe liver mass. The subject received previous radiotherapy toT6, T10, L1 and L3. Previous anticancer therapy included gemcitabine, docetaxel, doxorubicin and ifosfamide. Prior and concomitant medications included acetylsalicylic acid, colecalciferol, escitalopram, lorazepam, magnesium, metoprolol, ondansetron, paracetamol, prochlorperazine, unspecified herbal and traditional medicine, vicodin and vitamins. ECOG performance status at screening was 1

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 21), the subject was hospitalized for worsening atrial fibrillation (Grade 3). On physical examination, her heart beat was fast and irregular. ECG showed atrial fibrillation at 126 beats per minute. The subject was treated with flecainide. The subject recovered on [redacted] (Day 22). The Investigator considered worsening atrial fibrillation serious and not related to the study drug.

On [redacted] (Day 81), the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 67).

被験者番号	11231004
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	汎血球減少症/Pancytopenia[注)]

注）当該被験者の重篤な有害事象は，貧血/Anaemia，好中球減少症/Neutropenia，血小板数減少/Platelet count decreasedとして集計されている。

A 54-year-old white male was diagnosed with intermediate grade dedifferentiated adipocytic sarcomain retroperitoneum on 05 Oct 2009. The last date of disease progression was 15 Mar 2012. Significant medical history included, aortic stenosis, type 2 diabetes mellitus, holosystolic murmur, hydronephrosis, hypertension, hypoalbuminaemia, left femoral neuropathy, peripheral motor neuropathy, stomatitis, pleural effusion, proteinuria, pulmonary hypertension, resection of left retroperitoneal sarcoma and left colectomy with mobilization of splenic flexure, retroperitoneal abscess, bipedal edema, neutropenia, retroperitoneal mass, arthralgia and transient paresthesias. At Screening, tumor assessments of target/non-target lesions via CT scan showed anterior abdominal lesion and lateral posterior retroperitoneal lesion. The subject received previous radiotherapy to left abdominopelvic region and retroperitoneal resection bed. Previous anticancer therapy included gemcitabine, docetaxel, doxorubicin, and ifosfamide. Prior and concomitant medications included filgrastim, furosemide, gabapentin, insulin aspart, insulin detemir, metformin, ondansetron, pegfilgrastim, prochlorperazine, stomatologicals and mouth preparations. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 21), the subject experienced anemia (Grade 3), stomatitis (Grade 2), hypocalcemia (Grade 1), neutropenia (Grade 3), contusion (Grade 1), decreased white blood cell (WBC) (Grade 3) and decreased platelet count (Grade 4). Laboratory results showed platelet count of 9 x10^9/L (NR: 125-375), WBC count of 1.1 x10^9/L (NR: 3.7-11), RBC count of 2.95 x10^9/L (NR: 4-5.6), hemoglobin 75 g/L (NR: 125 – 170) and the study drug was interrupted. The subject was transfused with red blood cells and platelets. The subject recovered from stomatitis, contusion, decreased WBC count on [redacted] (Day 50). He recovered from hypocalcaemia and decreased platelet count on [redacted] (Day 31), from neutropenia on [redacted] (Day 38) and anemia was ongoing. The Investigator considered anemia, neutropenia and decreased platelet count serious and probably related to the study drug and stomatitis, contusion, hypocalcemia and decreased white blood cell count non-serious and probably related to the study drug.

On [redacted] (Day 50), the subject experienced ongoing anemia (Grade 2) and hematuria (Grade 1) with hemoglobin of 81g/L. On the same day, the study drug dose was reduced to 850 mg/m^2 due to these events. The subject did not recover from both these events. The Investigator considered anemia non-serious and probably related to the study drug and hematuria non-serious and possibly related to the study drug.

On [redacted] (Day 81), the subject experienced increased blood alkaline phosphatase (Grade 1), decreased white blood cell count (Grade 2), decreased neutrophil count (Grade 2), decreased lymphocyte count (Grade 2) and hyponatremia (Grade 1). Laboratory results showed WBC of 2.7 x10^9/L and sodium level of 137 mmol/L (NR: 133-145). On the same day, the study drug dose was reduced to 680 mg/m^2 due to these events and the subject received the last dose of the study drug. On [redacted] (Day 113), the subject recovered from decreased white blood cell count, decreased lymphocyte count and decreased neutrophil counts. The subject did not recover from increased alkaline phosphatase and hyponatremia. The Investigator considered all the events non-serious and probably related to the study drug.

On [redacted] (Day112), the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 81).

被験者番号	11271006
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	十二指腸瘻/Duodenal fistula

A 65-year-old african-american female was diagnosed with high grade dedifferentiated adipocytic sarcoma in retroperitoneum on 25 Jun 2012. The last date of disease progression was 17 Jan 2013. Significant medical history included bilateral elbow surgery, diabetes mellitus, endometriosis, bone pain, hyperlipidemia, hypertension, hypocalcaemia, hypokalemia, pruritus, laparoscopic hysterectomy, tumor pain, peripheral edema, nephrostomy, central venous catheterization, and pulmonary embolism. At Screening, tumor assessments of target/non-target lesions via CT scan showed retroperitoneal mass, left retroperitoneal nodule and right psoas nodule. Previous anticancer therapy included gemcitabine, docetaxel, doxorubicin, and investigational drug th-302. Prior and concomitant medications included acetylsalicylic acid, dexamethasone, diphenhydramine, dronabinol, emla, enoxaparin, fosaprepitant, hydrocortisone, hydromorphone, hydroxyzine, ibuprofen, insulin glargine, loratadine, lorazepam, macrogol, magnesium sulfate, metronidazole, morphine, norepinephrine, ondansetron, potassium, prochlorperazine, promethazine, red blood cells, senna alexandrina and sodium chloride. ECOG performance status at screening was 2.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 24), the subject experienced diarrhea (Grade 4). On [redacted] (Day 25), the subject was hospitalized for duodenal fistula (Grade 3) and dehydration (Grade 4) with blood pressure of 80/40 mm Hg. The study drug was interrupted due to these events. The subject was treated with vancomycin, piperacillin/tazobactam, flucanozole, potassium, norepinephrine, metronidazole, sodium chloride and paracetomol. On [redacted] (Day 38), the subject experienced bilateral pleural effusion (unknown etiology) (Grade 1) and pericardial effusion (unknown etiology) (Grade 1). The subject recovered from dehydration on [redacted] (Day 42) and from duodenal fistula on [redacted] (Day 45). The subject did not recover from diarrhea and pericardial effusion and was reported recovering from bilateral pleural effusion. On [redacted] (Day 42), the subject was withdrawn from the study due to clinical disease progression and received the last dose of the study drug on [redacted] (Day 22). The Investigator considered duodenal fistula serious and not related to the study drug; dehydration non-serious and probably related to the study drug, pleural effusion, pericardial effusion and diarrhea non-serious and not related to the study drug, but related to the disease.

被験者番号	11291005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	ヘモグロビン減少/Hemoglobin decreased
治験薬の投与中止に至った有害事象	疲労/Fatigue

A 65-year-old white male was diagnosed with high grade pleomorphic liposarcma in retroperitoneum on 11 Aug 2006. The last date of disease progression was 21 Oct 2011. Significant medical history included cholecystecotmy, dysphagia, incisional hernia repair, knee arthroscopy, left nephrectomy, sarcoma excision and retroperitoneal tumor debulking. At Screening, tumor assessments of target/non-target lesions via CT scan showed central retroperitoneal lesion, lesions adjacent to descending colon, and adjacent to left psoas and left retroperitoneal lesion. The subject received previous radiotherapy to bladder mass. Previous anticancer therapy included tasisulam, doxorubicin, ifosfamide, sorafenib, trabectedin and troglitazone. Prior and concomitant medications included citalopram, cod-liver oil, dexamethasone, lorazepam, omeprazole, ondansetron, prochlorperazine and ranitidine. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 2), the subject experienced fatigue (Grade 1) and on [redacted] (Day 57), the severity increased to Grade 2. Due to its persistence, on [redacted] (Day 77), the study drug was withdrawn and the subject received the last dose of the study drug on the same day. The Investigator considered fatigue non-serious and possibly related to the study drug.

On [redacted] (Day 88), the subject experienced decreased hemoglobin (Grade 3). Laboratory results showed hemoglobin of 7.3 g/dL (NR: 12.5-17) and hematorcrit 23.6% (NR: 37-51.0). The subject was given blood transfusion and he recovered from this event on [redacted] (Day 136). The Investigator considered this event serious (important medical event) and probably related to the study drug.

The subject was withdrawn from the study on [redacted] (Day 128) due to ongoing fatigue.

被験者番号	11361001
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腹痛/Abdominal pain，大腸閉塞/Large intestinal obstruction

A 50-year-old white male was diagnosed with high grade leiomyosarcoma on 23 Feb 2010. The last date of disease progression was 13 Jan 2012. Significant medical history included abdominal hernia, urticarial, umbilical hernia, abdominal pain, small intestinal resectionexploratory laparotomy, ileocecal resection and upper-airway cough syndrome. At Screening, tumor assessments of target/non-target lesions via CT scan showed right paracolic gutter mass, anterior left paramedial pelvic mass, intra-abdominal mass, pelvic omental mass and peritoneal mass. Previous anticancer therapy included doxorubicin, ifosfamide, gemcitabine and docetaxel. Prior and concomitant medications included aprepitant, dexamethasone, dexrazoxane, diphenhydramine, ibuprofen, lactulose, levofloxacin, macrogol, magnesium hydroxide, mesna, metoclopramide, metronidazole, ondansetron, palonosetron, paracetamol, phenylephrine, prochlorperazine and senokot. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 20), the subject experienced malignant ascites (Grade 2), nausea (Grade 2) and vomiting (Grade 1). On [redacted] (Day 21), he was hospitalized for large intestinal obstruction (Grade 3). The study drug was interrupted due to these events. CT scan of abdomen showed a large cystic mass. He underwent ultrasound guided left paracentesis and pigtail catheter placement. He was treated with dexamethasone, metoclopramide and ondansetron. He recovered on [redacted] (Day 22) from large intestinal obstruction and vomiting while malignant ascites and nausea were ongoing. The Investigator considered large intestinal obstruction serious and not related to the study drug; nausea non-serious and probably related to the study drug; malignant ascites non-serious and not related to the study drug; but related to the disease and vomiting non-serious and not related to the study drug.

On [redacted] (Day 44), the subject was hospitalized for abdominal pain (Grade 3). On the same day, the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 37). He was treated with morphine, oxycodone and hydromorphone. He recovered on [redacted] (Day 48). The Investigator considered abdominal pain serious and not related to the study drug.

被験者番号	11381002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	下痢/Diarrhea，発熱/Pyrexia，小腸閉塞/Small intestinal obstruction

A 52-year-old white male was diagnosed with high grade dedifferentiated liposarcoma in retroperitoneum on 10 Aug 2011. The last date of disease progression was 19 Mar 2013. Medical history included hemicolectomy, intra-cranial lesion excision, gastritis, hemorrhoids, hydronephrosis, migraine, resection of abdominal mass, resection of illiac mass and retroperitoneal pain. At Screening, tumor assessments of target/non-target lesions via MRI showed retroperitoneal mass and left lingular lobe lung mass. The subject received previous radiotherapy to retroperitoneum. Previous anticancer therapy included gemcitabine, docetaxel, doxorubicin and ifosfamide. Prior and concomitant medications included cefalexin, docusate, famotidine, hydromorphone, ketorolac, lactulose, lorazepam, metoclopramide, mirtazapine, morphine, naloxone, ondansetron, oxycocet, paracetamol, red blood cells, sodium chloride and vancomycin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 16), the subject was hospitalized for small intestinal obstruction (Grade 3). On [redacted] (Day 18), he experienced wound dehiscence (Grade 2). The study drug was interrupted due to wound dehiscence. He underwent CT scan of the abdomen with small bowel resection, G-tube placement, entero-colostomy and G-tube clamped. He was treated with diphenhydramine, cephalexin and heparin. He recovered from small intestinal obstruction on [redacted] (Day 23) and from wound dehiscence on [redacted] (Day 42). The Investigator considered small intestinal obstruction serious and not related to the study drug and wound dehiscence non-serious and not related to the study drug. The study drug was resumed on [redacted] (Day 43).

On [redacted] (Day 77), the subject was hospitalized for pyrexia (Grade 2) and diarrhea (Grade 3). On the same day, the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 64). He was treated with lomotil, cefepime and metronidazole. The subject recovered from pyrexia on [redacted] (Day 78) and from diarrhea on [redacted] (Day 81). The Investigator considered pyrexia and diarrhea serious and not related to the study drug.

被験者番号	11391004
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	血小板減少症/Thrombocytopenia

A 63-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 16 Dec 2010. The last date of disease progression was 01 Jul 2012. Significant medical history included cervical cord compression, decreased motor strength, muscular weakness and exercise-induced asthma. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe liver mass, left upper lobe and right lower lobe lung masses, bone lesion, multiple liver metastases and multiple pulmonary metastases. The subject received previous radiotherapy to cervical vertebral lesion C4-8 and T12-L2. Previous anticancer therapy included gemcitabine, docetaxel, doxorubicin, , antineoplastic agents and trabectedin. Prior and concomitant medications included aprepitant, calcium w/vitamin D, dexamethasone, filgrastim, granisetron, ibuprofen, lorazepam, omeprazole, ondansetron, palonosetron, pegfilgrastim and salbutamol. ECOG performance status at screening was 2.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 37), the subject experienced neutropenia (Grade 2), leukopenia (Grade 3) and thrombocytopenia (Grade 4). Laboratory results showed absolute neutrophil count of 1.4 x 10^9/L (NR: 1.7 – 7/9), white blood cell count of 1.8 x10^9/L (NR: 3.7-11) and platelet count of 20 x 10^9/L (NR: 125 – 375). On [redacted] (Day 44), the thrombocytopenia improved to Grade 2 with platelet counts 53 x10^9/L. She was transfused with platelets and treated with filgrastim and recovered from neutropenia, leukopenia and thrombocytopenia on [redacted] (Day 51). On the same day, the study drug dose was reduced to 850 mg/m^2 due to these events. The Investigator considered thrombocytopenia serious and probably related to the study drug; neutropenia and leukopenia non-serious and probably related to the study drug.

On [redacted] (Day 92), the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 72).

被験者番号	11991005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	好中球減少症/Neutropenia，血小板減少症/Thrombocytopenia

A 67-year-old white female was diagnosed with high grade leiomyosarcoma in bones and joints on 08 Dec 2010. The last date of disease progression was 14 Jun 2012. Medical history included reconstruction of right proximal tibia utilizing prosthetic stryker modular replacement system, total knee replacement, cystopexy, metastatic pain, peripheral edema, grand mal convulsion, hyperlipidemia, hysterectomy, post-surgical hypotension, urethral prolapse, pulmonary embolism, right knee proximal tibial sarcoma excision and right proximal tibia biopsy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right upper and lower lobe lung mass, multiple bilateral pulmonary nodules, multiple liver lesions not confined to one quadrant and multiple bone lesions not confined to one region. Previous anticancer therapy included doxorubicin, trabectedin, gemcitabine and docetaxel. Prior and concomitant medications included colecalciferol, dalteparin, docusate, loratadine, lorazepam, macrogol, magnesium hydroxide, ondansetron, pegfilgrastim, phenytoin, prochlorperazine, senna alexandrina, simvastatin, vitamins and zoledronic acid. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15), the subject experienced thrombocytopenia (Grade 4) and neutropenia (Grade 4) with platelet count of 30 x10^9/L (NR: 125-375) and neutrophil count of .0.46 x10 ^9/L (NR: 1.7 – 7.9). The subject received platelet transfusion. The subject recovered from thrombocytopenia on [redacted] (Day 28) and from neutropenia on [redacted] (Day 22). The Investigator considered neutropenia and thrombocytopenia serious and probably related to the study drug. On [redacted] (Day 29), the study drug dose was reduced to 850 mg/m^2 due to thrombocytopenia.

On [redacted] (Day 36), the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 29).

被験者番号	12011003
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	深部静脈血栓症/Deep vein thrombosis

A 58-year-old white male was diagnosed with high grade leiomyosarcoma in connective and soft tissue on 08 Jun 2009. The last date of disease progression was 27 Sep 2011. Significant medical history included hemoptysis, pulmonary embolism, hypercholesterolemia, hypertension, nephrectomy and dyspnea. At Screening, tumor assessments of target/non-target lesions via CT scan showed right pericardiac/perihilar mass, right pleural mass and multiple bilateral lung nodules. The subject received previous radiotherapy to the right thigh. Previous anticancer therapy included gemcitabine, docetaxel, and doxorubicine. Prior and concomitant medications included dalteparin, metronidazole, platelets and vancomycin. ECOG performance status at screening was 2.

On [redacted] (Day -11), the subject was hospitalized for pulmonary embolism (Grade 3). He underwent IVC filter placement and treated with heparin. He recovered on [redacted] (Day -9). The Investigator considered pulmonary embolism serious and not related to the study drug.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 14), the subject experienced thrombocytopenia (Grade 3) and was transfused with platelets. He recovered from this event on [redacted] (Day 28). The Investigator considered this event non-serious and probably related to the study drug. The study drug dose was reduced to 900 mg/m^2 on [redacted] (Day 29) due to this event.

On [redacted] (Day 34), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received last dose of the study drug on [redacted] (Day 29).

On [redacted] (Day 46), the subject was hospitalized for deep vein thrombosis (Grade 3). Imaging confirmed deep venous thrombosis. He did not recover from this event. The Investigator considered deep vein thrombosis serious and not related to the study drug.

被験者番号	12021002
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	悪性胸水/Malignant pleural effusion，汎血球減少症/Pancytopenia
治験薬の投与中止に至った有害事象	悪性胸水/Malignant pleural effusion

A 51-year-old african-american female was diagnosed with intermediate grade pleomorphic liposarcoma on 27 Sep 2010. The last date of disease progression was 17 Jul 2012. Medical history included non-cardiac chest discomfort, left back pain, left pneumothorax, partial excision of tumor on the left thigh, pleuroscopy and sarcoma excision. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lung mass, left pleural mass, right pleural mass, left lobe liver mass, right lobe liver mass and multiple cervical vertebral mass. The subject received previous radiotherapy to left thigh. Previous anticancer therapy included IPM3001 (investigational drug), gemcitabine and trabectedin. Concomitant medications included calcium, dalteparin, denosumab, glycerol, oxycocet, oxycodone, paracetamol, prochlorperazine, senna alexandrina, and vitamin D. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 14), the subject was hospitalized for malignant pleural effusion (Grade 3), pancytopenia (Grade 3), and tachycardia (Grade 3). Laboratory results showed white blood cell (WBC) count 6.19 x10^9/L (NR: 3.7-11), platelets count of 67 x10^9/L (NR: 125-375), hemoglobin of 66 g/L (NR: 110-155). The study drug was withdrawn due to malignant pleural effusion. The subject received the last dose of the study drug on [redacted] (Day 1). The subject underwent thoracocentesis with Tenckhoff drain. The subject was treated with oxycocet, two units of red blood cells and one unit of platelets and recovered on [redacted] (Day 24). On [redacted] (Day 29), the tumor response assessment showed disease progression and the subject was withdrawn from the study. The Investigator considered malignant pleural effusion, pancytopenia serious and not related to the study drug and tachycardia non-serious and not related to the study drug.

被験者番号	12021005
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	胆管炎/Cholangitis，胆嚢炎/Cholecystitis

A 61-year-old white female was diagnosed with intermediate grade leiomyosarcoma in the uterus on 20 Jan 2000. The last date of disease progression was 14 Nov 2012. Significant medical history included deep vein thrombosis, li-fraumeni syndrome, carpal tunnel syndrome, bilateral salpingo-oophorectomy, hypothyroidism, irritable bowel syndrome, laparotomy, metastases to biliary tract, omentectomy, pelvic and periaortic lymphadenectomy, peripheral sensory neuropathy, thyroid papillary carcinoma, total abdominal hysterectomy and total thyroidectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lung lobe and right upper lobe lung mass and porta hepatis. The subject had previous radiotherapy to uterine mass. Previous anticancer therapy included gemcitabine, doxorubicin, ifosfamide, and trabectedin. Prior and concomitant medications included calcium carbonate, docusate, levothyroxine, ondansetron, pantoprazole, paracetamol, prochlorperazine and ranitidine. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 70), the subject was hospitalized for cholecystitis (Grade 3). The subject underwent percutaneous cholecystotomy tube placement and drainage. She recovered on [redacted] (Day 76). The study drug dose was not changed. The Investigator considered cholecystitis serious and not related to the study drug.

On [redacted] (Day 80), the subject was hospitalized for cholangitis (Grade 3). Laboratory results showed aspartate aminotransferase (AST) of 511U/L (NR: 10-43); alanine transaminase (ALT) of 259U/L (NR: 10-40); alkaline phosphatase of 1350U/L (NR: 30-115). She underwent endoscopic retrograde cholangio-pancreatography and plastic stent was placed. The subject recovered on [redacted] (Day 88). The Investigator considered cholangitis serious and not related to the study drug.

On [redacted] (Day 95), the subject was hospitalized for tumor pain (Grade 3). The study drug was withdrawn due to tumor pain and the subject received the last dose of the study drug on [redacted] (Day 50). On [redacted] (day 98), the subject was withdrawn from the study due to this event. She recovered from this event on [redacted] (Day 101). The Investigator considered tumor pain serious and not related to the study drug.

被験者番号	14031001
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	蜂巣炎/Cellulitis、深部静脈血栓症/Deep vein thrombosis
治験薬の投与中止に至った有害事象	疲労/Fatigue

A 31-year-old white female was diagnosed with intermediate grade dedifferentiated liposarcoma in retroperitoneum on 28 Apr 2009. The last date of disease progression was 03 Apr 2012. Significant medical history included descending hemicolectomy, tumur excision, tumor pain, left adrenalectomy, splenectomy, left ovarian cystectomy, resection of retroperitoneal liposarcoma, adhesiolysis and peripheral swelling. At Screening, tumor assessments of target/non-target lesions via CT scan showed left retroperitoneal mass, fat density lesion involving left common femoral vessels, fat density lesion lying to the right and adjacent to the descending duodenum, soft tissue mass within the left peritoneum and soft tissue mass in superficial inguinal region. Previous anticancer therapy included epirubicin, ifosfamide, everolimus, and trabectadin. Prior and concomitant medications included granisetron, oxycodone and sodium bicarbonate. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 5), the subject was hospitalized for cellulitis (Grade 3). On the following day, on physical examination the subject was found to have increased leg pain (Grade 2) and left leg swelling (Grade 2). She was treated with sertraline, lorazepam, oxycodone, mirtazapine, cephalexin, meropenem, enoxaparin, amoxicillin, vancomycin, fentanyl, nystatin, temazepam and promethazine. On [redacted] (Day 8), the subject recovered from cellulitis. She recovered from left leg swelling and leg pain on [redacted] (Day 9). On the same day, the subject experienced fatigue (Grade 2) and did not recover from this event. The Investigator considered cellulitis serious and possibly related to the study drug; fatigue non-serious and possibly related to the study drug; leg pain and left leg swelling non serious and not related to the study drug.

On [redacted] (Day 37), the subject experienced fatigue (Grade 3). The study drug was interrupted due to this event. She recovered on [redacted] (Day 52). The Investigator considered fatigue non-serious and possibly related to the study drug. On [redacted] (Day 53), the study drug was resumed.

On [redacted] (Day 56), the subject was hospitalized for deep vein thrombosis (Grade 3) which was confirmed by ultrasound of the lower limbs. She was treated with sertraline, oxycodone, mirtazapine, acetylsalicyclic acid, enoxaparin, fentanyl, paracetamol, cephalexin, nystatin, coloxyl with senna, ondansetron, movicol, metoclopramide, dexamethasone, mylanta and clindamycin. She recovered on [redacted] (Day 64). The Investigator considered deep vein thrombosis serious and not related to the study drug.

On [redacted] (Day 87), the subject experienced fatigue (Grade 3), left leg pain (Grade 2), and left leg swelling (Grade 3). The study drug was withdrawn due to fatigue. The subject received the last dose of the study drug on [redacted] (Day 86). She was treated with enoxaparin. On [redacted] (Day 128), the subject recovered from fatigue and did not recover from leg pain and left leg swelling. The Investigator considered fatigue non-serious and possibly related to the study drug; left leg swelling and left leg pain non-serious and not related to the study drug.

被験者番号	17011001
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anemia，脊椎痛/Spinal pain
治験薬の投与中止に至った有害事象	貧血/Anemia

A 61-year-old white male was diagnosed with high grade pleomorphic liposarcoma of the left buttock on 15 Oct 2010. The last date of disease progression was 05 Jun 2012. Significant medical history included acute nephritis, tonsillectomy, asbestosis, tumor excision, fatigue, folium deficiency, inguinal hernia, intermittent anemia grade 1, sarcoma excision, pneumothorax, thoracoscopy and tumor pain. At Screening, tumor assessments of target/non-target lesions via CT scan showed right upper lobe and left lower lobe lung mass. The subject received previous radiotherapy to left gluteal region. Previous anticancer therapy included doxorubicine, palifosfamide/ placebo and trabectedine. Prior and Concomitant medications included alprazolam, bacillus clausii, blood cells, dexamethasone, dulcodos, enoxaparin, escitalopram, fentanyl, folic acid, furosemide, lidocaine, lorazepam, lormetazepam, methylprednisolone, metoclopramide, movicol, naproxen, pantoprazole, paracetamol, pregabalin, spironolactone, tinzaparin, tramadol, trazodone and tropisetron. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated

On [redacted] (Day 23), the subject experienced anemia (Grade 2) with hemoglobin level 94 g/L (NR: 125-170). On [redacted] (Day30), the anemia recovered. The Investigator considered anemia was non-serious and probably related to the study drug.

On [redacted] (Day 43), the subject was hospitalized for anemia (Grade 2) with hemoglobin of 91g/L and hematocrit of 29% (NR: 37-51). The study drug was withdrawn due to anemia. The subject received the last dose of the study drug on [redacted] (Day 23). The subject was given 2 units of packed red blood cells and recovered on [redacted] (Day 45). The study drug was withdrawn due to anemia and the subject received the last dos eof the study drug on [redacted] (Day 23). The subject was withdrawn from the study due to clinical disease progression. The Investigator considered anemia serious and probably related to the study drug.

On [redacted] (Day 51), the subject was hospitalized for paravertebral pain (Grade 3) and was treated with morphine and diclofenac. The subject recovered with sequelae from paravertebral pain on [redacted] (Day 65). The Investigator considered paravertebral pain serious and not related to the study drug.

被験者番号	17021002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	好中球数減少/Neutrophil count decreased, 血小板減少症/Thrombocytopenia

A 62-year-old white male was diagnosed with high grade leiomyosarcoma in adrenal glands on 02 Sep 2009. The last date of disease progression was 25 Oct 2011. Significant medical history included anemia, decreased neutrophil count , lymphopenia, thrombocytopenia, vascular hamartoma, hepatic, renal, splenic and pancreatic cyst, emphysema, exertional dyspnea, hypotension and goiter. At Screening, tumor assessments of target/non-target lesions via CT scan showed right middle lobe, left upper and lower lobe lung masses. Previous anticancer therapy included doxorubicine and ifosfamide. Prior and concomitant medications included alizapride, dexamethasone and ondansetron. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 22), the subject experienced decreased neutrophil count (Grade 1) and thrombocytopenia (Grade 1) with neutrophil count of 1.4 x 10^9 (NR: 1.7 – 7.9) and platelet count of 58 x 10^9/L ((NR: 125 – 375). On [redacted] (Day 43), the thrombocytopenia worsened to Grade 3 with platelet count of 27 x 10^9/L. On [redacted] (Day 47), the thrombocytopenia worsened to Grade 4 and decreased neutrophil count worsened to Grade 3 with neutrophil count of 1.0 x10^9/L. The study drug was interrupted due to thrombocytopenia. The subject was transfused with packed blood cells and he recovered on [redacted] (Day 56) from thrombocytopenia. On [redacted] (Day 57), the decreased neutrophil count improved to grade 1. On the same day, the study drug was resumed at a reduced dose of 850 mg/m^2. The subject did not recover from decreased neutrophil count. The Investigator considered thrombocytopenia and decreased neutrophil count serious (important medical events) and probably related to the study drug.

On [redacted] (Day 78), the tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 57).

被験者番号	17021008
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anemia，白血球減少症/Leukopenia，好中球減少症/Neutropenia，発熱/Pyrexia

A 54-year-old white female was diagnosed with high grade leiomyosarcoma in pancreas on 31 Jul 2009. The last date of disease progression was 20 Mar 2012. Medical history included mass excision, partial small intestine resection, resection of intra-abdominal mass relapse and pancreaticoduodenectomy. At Screening, tumor assessments of target/non-target lesions showed lesions in right pelvis and left flank and right kidney mass. Previous anticancer therapy included doxorubicine and ifosfamide. Prior and concomitant medications included ibuprofen, lormetazepam and tinzaparin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 43), the subject experienced leukopenia (Grade 3) with white blood cell (WBC) count of 1.6 x 10^9/L (NR: 3.7 – 11) and neutropenia (Grade 3) with neutrophil count of 0.9 x 10^9/L (NR: 1.7 – 7.9). The study drug was interrupted due to leukopenia and resumed on [redacted] (Day 49).

On [redacted] (Day 113), the subject experienced leukopenia (Grade 3) with WBC count of 1.8 x 10^9/L and neutropenia (Grade 3) with neutrophil count of 0.8 x10^9/L. The study drug was interrupted due to leukopenia and resumed on [redacted] (Day 121).

On [redacted] (Day 141), the subject was hospitalized for neutropenia (Grade 3), anemia (Grade 2), pyrexia (Grade 1) and leukopenia (Grade 3). On the same day, tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 121). Laboratory results showed RBC count of 2.5 x10^9/L (NR: 3.7-5.2), absolute neutrophil count of 0.5 x10^9/L (NR: 1.7-7.9), WBC count of 1.2 x10^9/L and hemoglobin of 89 g/L (NR: 110-155). The study drug was interrupted due to leukopenia. She was transfused with packed red blood cells and treated with piperacillin/tazobactam. The subject recovered from pyrexia and leukopenia on [redacted] (Day 145), from neutropenia on [redacted] (Day 154) and from anemia on [redacted] (Day 167). The Investigator considered anemia, leukopenia, pyrexia and neutropenia serious and probably related to the study drug.

被験者番号	17021016
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	好中球減少症/Neutropenia

A 38-year-old white female was diagnosed with intermediate grade dedifferentiated liposarcoma in mediastinum on 23May 2012. The last date of disease progression was on 08 Apr 2013. Significant medical history included anemia, constipation, gastric ulcer, dyspnea, thyroidectomy, irritable bowel syndrome, non-cardiac chest pain, and tumor pain. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in mediastinum, left lower lobe of lung and base of left lung. Previous anticancer therapy included doxorubicin and ifosfamide. Prior and concomitant medications included artificial tears, betamethasone, buprenorphine, clobetasol, domperidone, enoxaparin, levothyroxine, movicol, ofloxacin, ondansetron, oxycodone, oxytetracycline, paracetamol/codeine, pantoprazole, paracetamol, targin, tramadol and vaccinium macrocarpon. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 21), the subject experienced neutropenia (Grade 3) with absolute neutrophil count (ANC) of 0.6 x 10^9/L (NR: 2.5-7.8). On [redacted] (Day 43), the subject recovered from this event with ANC 2.2 x 10^9/L. On the same day, the study drug dose was reduced to 850 mg/m^2 due to this event. The Investigator considered neutropenia serious (important medical event) and probably related to the study drug.

On [redacted] (Day 106), the subject experienced neutropenia (Grade 3) with neutrophil count of 0.9 x 10^9/L. The study drug was interrupted due to this event. The Investigator considered neutropenia non-serious and probably related to study drug

On [redacted] (Day 138), tumor response assessment showed disease progression and the subject was withdrawn from study. The last dose of the study drug was received on [redacted] (Day 113).

被験者番号	18011003
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	発熱/Pyrexia

A 54-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 08 Apr 2008. The last date of disease progression was 06 Aug 2012. Medical history included ulcerative colitis, fatigue and abdominal pain. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in peritoneal/omental mass. Previous anticancer therapy included doxorubicin, gemcitabine, ifosfamide, belinostat and paclitaxel. Prior and concomitant medications included domperidone, loperamide, morphine, palonosetron, paracetamol and prednisolone. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 28), the subject was hospitalized for pyrexia (Grade 1) with temperature of 38.5 degree Celsius (NR: 36.5-37.2). On the same day, the subject had anemia (Grade 2) with hemoglobin 90 g/L (NR: 110 – 155) and tachycardia (Grade 1) with blood pressure 108/51 mmHg and heart rate of106/min. No obvious source of infection was found. She was treated with RBC transfusion, piperacillin/tazobactam and phenoxymethylpenicillin. On [redacted] (Day 30), the subject recovered from pyrexia and tachycardia and from anemia on [redacted](Day 35). The Investigator considered pyrexia serious and not related to the study drug; anemia non-serious and possibly related to the study drug; tachycardia non-serious and not related to study drug.

On [redacted] (Day 37), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 25).

被験者番号	19011003
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	丹毒/Erysipelas

A 57-year-old male was diagnosed with high grade myxoid liposarcoma in left ankle on 12 Aug 2010. The last date of disease progression was 03 Aug 2012. Medical history included coronary arterial stent insertion, myocardial ischemia and pericarditis. At Screening, tumor assessments of target/non-target lesions via CT scan showed mesenteric basis lesion, mediastinum nodule, left lateral lobe segment II liver mass, right upper lobe lung mass and mediastinal thoracic adenopathy. The subject received previous radiotherapy to left ankle and previous anticancer therapy included doxorubicin, ifosfamide and trabectedin. Prior and concomitant medications included aprepitant, diltiazem, esomeprazole, fentanyl, hydroxyzine, morphine, nefazan compuesto, ondansetron, paroxetine, phloroglucinol and red blood cells. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 30), the subject was hospitalized for erysipelas of left lower limb (Grade 4). He was treated with paracetamol, piperacillin/tazobactam, ciprofloxacin, linezolid and enoxaparin. On the same day, tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 22). On [redacted] (Day 36), the subject recovered from this event. The Investigator considered erysipelas serious and not related to the study drug.

被験者番号	19041011
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	好中球減少症/Neutropenia

A 57-year-old male was diagnosed with intermediate dedifferentiated liposarcoma in retroperitoneum on 13 Oct 2011. The last date of disease progression was 19 Sep 2012. Medical history included left nephrectomy, appendectomy and arthroscopy. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in trunk and fat of the left hypochondrium. Previous anticancer therapy included doxorubicin, protein kinase inhibitors and trabectedin. Prior andconcomitant medications included calcium, filgrastim, loperamide, metopimazine, probiotics and tinzaparin. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 22), the subject experienced neutropenia (Grade 4) with neutrophil count 0.3 x10^9/L (NR: 1.7-7.9). The study drug was interrupted due to neutropenia. On [redacted] (Day 29), the subject recovered from neutropenia and on the study drug was resumed. The Investigator considered neutropenia serious (important medical event) and probably related to the study drug.

On [redacted] (Day 113), the subject experienced neutropenia (Grade 3). On [redacted] (Day 131), the study drug dose was reduced to 800 mg/m^2 due to this event. He was treated with filgrastim and recovered from this event on [redacted] (Day 136). The Investigator considered neutropenia non-serious and possibly related to the study drug.

On [redacted] (Day 152), the subject experienced thrombocytopenia (Grade 1) with platelet count 98 x 10^9/L (NR: 125 – 375) and the study drug dose was further reduced to 600 mg/m^2, due to this event. The subject recovered from this event on [redacted] (Day 179). The Investigator considered thrombocytopenia non-serious and possibly related to the study drug.

On [redacted] (Day 313), tumor response assessment showed disease progression. On [redacted] (Day 320), the subject was withdrawn from the study due to disease progression and received the last dose of study drug.

被験者番号	19041014
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	医療機器関連感染/Device related infection，下痢/Diarrhea，発熱/Pyrexia，血小板減少症/Thrombocytopenia
治験薬の投与中止に至った有害事象	血小板減少症/Thrombocytopenia

A 59-year-old female was diagnosed with intermediate grade dedifferentiated liposarcoma in retroperitoneum on 12 Dec 2008. The last date of disease progression was 07 Dec 2012. Medical history included abdominal pain, appendectomy, tumor pain, dedifferenciated liposarcoma excision, adrenalectomy, dyspnea, sleep disorder, intestinal obstruction, breast lump removal, right nephrectomy, right colectomy and prosthetic vessel implantation. At Screening, tumor assessments of target/non-target lesions via CT scan showed soft tissue left and right abdominal masses, lesion in right iliac fossa and pelvic peritoneal effusion. The subject received previous radiotherapy to operative cavity and previous anticancer therapy included doxorubicin, ifosfamide, gemcitabine, and trabectedin. Prior and concomitant medications included amoxicillin, antacids, bromazepam, cortisone, domperidone, enemas, esomeprazole, fentanyl, furosemide, gentamicin, haloperidol, helicidine, lormetazepam, macrogol , magne-b6 mineral supplement , methylprednisolone, morphine, ofloxacin, omeprazole, paracetamol, prednisolone, pregabalin, primaxin, solutions for parenteral nutrition, sterculia urens, tinzaparin and tixocortol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 12), the subject was hospitalized for diarrhea (Grade 2) and was treated with corticosteroids. The subject recovered and was discharged from the hospital on the same day. The Investigator considered diarrhea serious and possibly related to the study drug;

On [redacted] (Day 15), the subject was hospitalized for pyrexia (Grade 3) which started as Grade 2 on [redacted] (Day 4). The subject's temperature was 38 degree celcius (NR: 36.5-37.2). She was treated with antibiotics. The subject recovered on [redacted] (Day 40). The Investigator considered pyrexia serious and possibly related to the study drug.

On [redacted] (Day 19), the subject was hospitalized for worsening catheter infection (Grade 3) which started as Grade 2 on [redacted] (Day 12). The subject was treated with ofloxacin, vancomycin, pristinamycin and recovered on [redacted] (Day 23). The Investigator considered device related infection serious and not related to the study drug.

On [redacted] (Day 47), the subject experienced thrombocytopenia (Grade 2). Laboratory results showed platelets 50 x 10^9/L (NR: 125-375). The study drug was interrupted due to this event. On [redacted] (Day 55), the subject was hospitalized for worsening thrombocytopenia (Grade 4). Laboratory results showed platelets 13 x10^9/L and the study drug was withdrawn due to this event. The subject received the last dose of the study drug on [redacted] (Day 27). The subject was treated with platelets transfusion. The subject did not recover from thrombocytopenia. The Investigator considered thrombocytopenia serious and probably related to the study drug.

被験者番号	19041018
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腸閉塞/Intestinal obstruction

A 47-year-old female was diagnosed with intermediate grade dedifferentiated liposarcoma in retroperitoneum on 18 Apr 2012. The last date of disease progression was 19 Feb 2013. Medical history included salpingo-oophorectomy, cholecystectomy, hypercholesterolaemia, nephrectomy, dyspnea, omentectomy, sarcoma excision, right colectomy and tumor pain. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in dome of hepatic, celiac and right hepatic. Previous anticancer therapy included doxorubicin, ifosfamide and trabectedin. Prior and concomitant medications included paracetomol, methylprednisolone, spasfon, trimebutine and pantoprazole. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 5), the subject was hospitalized for intestinal obstruction (Grade 3) associated with abdominal pain, acute spasms, nausea and vomiting. Radiological tests confirmed intestinal obstruction. The subject was treated with paracetamol, pantoprazole, methylprednisolone, osmotan, trimebutine and spasfon. On [redacted] (Day 9), the subject recovered from this event. The Investigator considered intestinal obstruction serious and not related to the study drug.

On [redacted] (Day 28), the subject experienced anemia (Grade 3) with hemoglobin of 79 g/L (NR: 110-155) and hematocrit of 24.9% (NR: 33-47). Her ECOG performance status was 2. She did not recover from anemia and the subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 1). The Investigator considered anemia non-serious and possibly related to the study drug.

被験者番号	19081006
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	呼吸困難/Dyspnoea，急性腎不全/Renal failure acute
病勢進行による死亡	不明

A 61-year-old male was diagnosed with high grade dedifferentiated adipocytic sarcoma in retroperitoneum on 04 Sep 2009. The last date of disease progression was 13 Jul 2012. Significant medical history included abdominal pain, inflammation, inguinal hernia, edema peripheral, raynaud's phenomenon, sarcoma excision, front of the psoas muscle operation, and right nephrectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed retroperitoneal mass, peritoneal/omental mass and hepatic lesion. Previous anticancer therapy included doxorubicin, carboplatin, cyclophosphamide, vindesine and trabectedin. Prior and concomitant medications included alprazolam, enoxaparin, esomeprazole, furosemide, general nutrients, haloperidol, macrogol 4000, magne-b6 oral, methylprednisolone, metoclopramide, morphine, ondansetron, paracetamol, prednisolone and spironolactone. ECOG performance status at screening was 2.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 7), the subject was hospitalized for dyspnea (Grade 2) and acute renal failure (Grade 1) associated with tachycardia, decreased appetite (Grade 3), abdominal pain (Grade 2), hypoalbuminaemia (Grade 2), hypertension (grade 3), testicular edema (Grade 1) and anxiety (Grade 2). Lab tests showed urea of 17.9 mmol/L (NR: 3.0-7.5), creatinine of 135 umol/L (NR: 62-124), creatinine clearance of 44.4 mL/min (NR: 85-125), and potassium of 4.2 mmol/L (NR: 3.5-5). The subject was treated with oxygen, oxycodone, enoxaparin, furosemide and potassium. The subject did not recover from these events. The Investigator considered dyspnea, and acute renal failure serious and not related to study drug; decreased appetite, abdominal pain, hypoalbuminaemia, hypertension, testisular edema, and anxiety non-serious and not related to the study drug.

On [redacted] (Day 10), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 1). On [redacted] (Day 16, 15 days after last dose), the subject died of unknown cause.

被験者番号	19081014
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	アラニンアミノトランスフェラーゼ増加/Alanine aminotransferase increased, アスパラギン酸アミノトランスフェラーゼ増加/Aspartate aminotransferase increased

A 58-year-old female was diagnosed with intermediate grade leiomyosarcoma in uterus on 24 Feb 2012. The last date of disease progression was 18 Jan 2013. Significant medical history included anemia, asthma, type 2 diabetes mellitus, back pain, hypertension, nausea, nausea, myomectomy, insomnia and vomiting. At Screening, tumor assessments of target/non-target lesions via CT scan showed pancreatic mass, liver mass, lung mass and bone lesions. The subject received previous radiotherapy to right iliac vertebrae (L3, L5) and sacral vertebrae (L2 to S1) and previous anticancer therapy included doxorubicin, gemcitabine and trabectedin. Prior and concomitant medications included aldactazine, alprazolam, aprepitant, domperidone, esomeprazole, fenofibrate, gliclazide, levocetirizine, macrogol, metformin, methylprednisolone, microlax morphine, movicol, ondansetron, paracetamol, prazepam, red blood cells, sterculia urens, stomatologicals mouth preparations and verapamil. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 42) the subject was hospitalized for increased alanine aminotransferase (ALT) (Grade 4) and increased aspartate aminotransferase (AST) (Grade 3). Laboratory results showed ALT level of 705 U/L (NR: 10-33) and AST level of 526 U/L (NR: 10 – 33). The subject recovered from increased AST on [redacted] (Day 62) and from increased ALT on [redacted] (Day 73). The Investigator considered these events serious and not related to the study drug.

On [redacted] (Day 46), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 21).

被験者番号	19081017
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	無気肺/Atelectasis

A 49-year-old female was diagnosed with high grade leiomyosarcoma in uterus on 25 Apr 2008. The last date of disease progression was 15 Mar 2013. Medical history included claustrophobia, constipation, cough, uterine leiomyoma embolisation, central venous catheterization, fatigue, hysterectomy, and bilateral oophorectomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed nodule in the lung lingula, right lower, upper and middle lobe lung masses and bone lesions. Previous anticancer therapy included doxorubicin, ifosfamide, cisplatin, ridaforolimus, gemcitabine and pazopanib. Prior and Concomitant medications included alprazolam, betamethasone, esomeprazole, methylprednisolone, ondansetron, oxyge and prazepam. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 34), the subject was hospitalized for atelectasis of right lung (Grade 3) associated with dyspnea. On [redacted] (Day 35), CT scan showed obstructive mass in the right bronchus secondary to metastases from uterine leiomyosarcoma, and also with increase in lung lesions. The subject was treated with oxygen, methylprednisolone and betamethasone. She recovered from this event on [redacted] (Day 38). The Investigator considered atelectasis serious and not related to the study drug,

On [redacted] (Day 42), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 21).

被験者番号	21011002
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	呼吸困難/Dyspnea

A 76-year-old white female was diagnosed with intermediate grade leiomyosarcoma in vagina and labia on 07 Mar 2008. The last date of disease progression was 23 Oct 2012. Significant medical history included chronic obstructive pulmonary disease, constipation, hysterectomy, left bundle branch block, abdominal distension, dyspnea, hypertension, left bundle branch block, left ventricular failure, anemia and diabetes mellitus. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in right upper and lower lobe of lung and right pleural effusion. The subject received previous radiotherapy to uterus and previous anticancer therapy included doxorubicin, gemcitabine and trabectedin. Prior and concomitant medications included amitriptyline, amlodipine, beloc-zoc comp, budesonide, clindamycin, dimeticone, metformin, metoclopramide, pantoprazole, piperacillin/tazobactam, primaxin, and torasemide. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 37), tumor response assessment showed disease progression and the subject was withdrawn from study. The last dose of the study drug was received on [redacted] (Day 22).

On [redacted] (Day 39), the subject was hospitalized for dyspnea (Grade 2). On the same day, hemoglobin was reported as 8.8 g/dL (NR: 11-15). The subject was transfused with red blood cells. On [redacted] (Day 59), the subject recovered with sequelae. The Investigator considered dyspnea serious and possibly related to the study drug.

被験者番号	21031002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	上腹部痛/Abdominal pain upper，筋骨格痛/Musculoskeletal pain，腫瘍疼痛/Tumour pain

A 53-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 04 Jul 2008. The last date of disease progression was 20 Dec 2012. Significant medical history included hypercoagulation, hypertension, adhesiolysis, excision of liver metastasis, increased alkaline phosphatase, hydronephrosis, spinal pain, left upper abdomen pain, pulmonary embolism, thrombectomy, omenectomy, deep vein thrombosis, ureterolysis procedure and prosthetic vessel implantation. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lower lobe lung mass, segment VII of liver mass, and lesions in trunk, both sides of pelvis and femur. Previous anticancer therapy included doxorubicin, carboplatin, docetaxel, gemcitabine, letrozole, mitomycin, pazopanib and trabectedin. Prior and concomitant medications included aprepitant, ceftriaxone, celecoxib, ciprofloxacin, dalteparin, dexamethasone, diclofenac, hydrochlorothiazide, lactulose, metamizole, metoclopramide, movicol, ondansetron, pantoprazole, pethidine, pregabalin, ramipril, tilidine, valoron n, zoledronic acid and zopiclone. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 12), the subject was hospitalized for tumor pain (Grade 3) and was treated with hydromorphone. On [redacted] (Day 16), the subject received palliative radiotherapy. On [redacted] (Day 17), the subject recovered with sequelae from this event. The Investigator considered this event serious and not related to the study drug.

On [redacted] (Day 91), the subject experienced worsening upper abdominal pain (Grade 2). On [redacted] (Day 97), the subject was hospitalized for worsening upper abdominal pain (Grade 3) and musculoskeletal pain (Grade 3) of left shoulder. The subject was treated with dexamethasone, fentanyl and morphine. On [redacted] (Day 105), the upper abdominal pain and musculoskeletal pain improved to Grade 2. The subject did not recover from these events. The Investigator considered these events serious and not related to the study drug.

On [redacted] (Day 115), the subject was hospitalized for right flank tumor pain (Grade 3). The subject was treated with morphine. On [redacted] (Day 121), the subject recovered with sequelae from this event. The Investigator considered tumor pain serious and not related to the study drug.

On [redacted] (Day 125), the subject was withdrawn from study due to clinical disease progression. The last dose of the study drug was received on [redacted] (Day 106).

被験者番号	21031004
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anemia

A 50-year-old white male was diagnosed with high grade leiomyosarcoma in right gluteus maximus on 17 Jul 2012. The last date of disease progression was 22 Jan 2013. Significant medical history included ataxia, anemia, astrocytoma, central nervous system lesion, spinal decompression, venous thrombosis limb, pulmonary embolism, spider naevus, biopsy metastasis at the back, metastasis excision at thoracic vertebra 9 and vestibular disorder. At Screening, tumor assessments of target/non-target lesions via CT scan showed right axillary thoracic adenopathy, lesion in cranial of the right kidney, liver masses in segment 2/4a and 7, right middle lobe lung mass, lesions in coracoid process, lumbar vertebra, right ilium, and sacrum, multiple retroperitoneale metastases and multiple mesenteriale metastases. The subject received previous radiotherapy to thoracic vertebra 8 – 10 and lower posterior trunk. Previous anticancer therapy included doxorubicin and ifosfamide. Prior and concomitant medications included aprepitant, dalteparin, dexamethasone, ondansetron, pantoprazole, pegfilgrastim, phenytoin and zoledronic acid. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 8), the subject was hospitalized for worsened anemia (Grade 4) with hemoglobin of 64 g/L (NR: 125-170). Endoscopic and colonoscopic evaluation ruled out gastrointestinal bleeding. He underwent infusion of red blood cell concentrate with iron and darbepoetin alfa. On [redacted] (Day 9), the subject recovered with sequelae from this event. The Investigator considered anemia serious and possibly related to the study drug.

On [redacted] (Day 44), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 22).

被験者番号	21041005
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anemia，鼻出血/Epistaxis，血小板減少症/Thrombocytopenia

A 53-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on Nov 2011. The last date of disease progression was 19 Feb 2013. Significant medical history included dyspnea, thromboembolectomy of left leg, hysterectomy with salpingo-oophorectomy and right thigh metastasis resection. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in right lung, left lower lobe and multiple areas of left lung. Previous anticancer therapy included docetaxel, gemcitabine, doxorubicin, ifosfamide, and trabectedin. Prior and concomitant medications included alizapride, clindamycin, dexamethasone, enoxaparin, erythropoietin human, granisetron, red blood cells and vitamin B12. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 81), the subject was hospitalized for epistaxis (Grade 4), thrombocytopenia (Grade 4) and anemia (Grade 4) secondary to epistaxis. Laboratory results showed platelet count 4 x10^9/L (NR: 125-375) and hemoglobin 54g/L (NR: 110-155). The study drug was interrupted due to epistaxis and thrombocytopenia. The subject underwent intranasal coagulation and was transfused with red blood cells and platelets. The subject recovered from epistaxis on [redacted] (Day 87). On [redacted] (Day 92), the subject recovered from thrombocytopenia and anemia improved to Grade 2. On [redacted] (Day 100), the study drug was resumed at a reduced dose of 1000 mg/m^2. On [redacted] (Day128), the subject recovered from anemia. The Investigator considered these events serious and possibly related to the study drug.

On [redacted] (Day 155), the subject was withdrawn from study due to clinical disease progression. The last dose of the study drug was received on [redacted] (Day 121). The subject died on [redacted] (Day 214, 73 days after the last dose) due to disease progression.

被験者番号	22011005
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	汎血球減少症/Pancytopenia

A 49-year-old white female was diagnosed with high grade dedifferentiated liposarcoma in retroperitoneum on 05 Jul 2011. The last date of disease progression was 03 Jul 2012. Medical history included cancer pain and lipoma excision. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions at paravertebral soft tissue, right upper lobe and right middle lobe lung masses, left upper lobe and left lower lobe lung masses. Previous anticancer therapy included doxorubicin, epirubicin, ifosfamide and trabectedin. Prior and concomitant medications included aprepitant, diclofenac, escitalopram, lactulose, lansoprazole, metoclopramide, nadroparin, oxycodone, paracetamol and pregabalin. ECOG performance status at screening was 2.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15), the subject was hospitalized for pancytopenia (Grade 4) and underwent blood and platelet transfusion. The subject was treated with piperacillin/tazobactam, fluconazole, filgrastim, teicoplanin and meropenem. The study drug dose was interrupted due to this event. On [redacted] (Day 37), the subject recovered from this event. The Investigator considered pancytopenia serious and probably related to the study drug.

On [redacted] (Day 50) the subject experienced anemia (Grade 2) with hemoglobin 85 g/L (NR: 110-155). On the same day, the study drug dose was resumed at a reduced dose of 670 mg/m^2 due to this event. She received blood transfusion on [redacted] (Day 51) and recovered from anemia on [redacted] (Day 100). The Investigator considered anemia non-serious and not related to the study drug.

On [redacted] (Day 58), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 50).

被験者番号	22031003
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	気胸/Pneumothorax
治験薬の投与中止に至った有害事象	気胸/Pneumothorax

A 64-year-old white female was diagnosed with high grade leiomyosarcoma in the retroperitoneum on 17 Sep 2009. The last date of disease progression was 26 Feb 2013. Medical history included glucose-6-phosphate dehydrogenase deficiency, hypothyroidism, allergy to metals and hypercholesterolemia. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe and left lower lobe lung masses, peritoneal/omental mass, pancreatic mass, lesions in peritoneum, paraesophageal sub-carinal lymphadenopathy and lesions in left inferior leg. Previous anticancer therapy included investigational drug, cisplatin, doxorubicin, ifosfamide, everolimus and sorafenib. Prior and concomitant medications included cefixime, dexamethasone, filgrastim, fusidic acid, granisetron, iruxol, lactobacillus reuteri, levothyroxine, nadroparin, omeprazole, paracetamol, penciclovir, pravastatin, ranitidine and valaciclovir. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 149), the subject was hospitalized for left pneumothorax (Grade 3) which was confirmed after chest and abdominal CT scan. The subject underwent a left thorax tube placement and the study drug was withdrawn. The subject received the last dose of the study drug on [redacted] (Day 142). The subject recovered on [redacted] (Day 168). The Investigator considered pneumothorax serious and probably related to the study drug.

被験者番号	22081002
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腸閉塞/Intestinal obstruction

A 65-year-old white female was diagnosed with intermediate grade leiomyosarcoma in ovary on 28 May 2007. The last date of disease progression was 06 Nov 2012. Significant medical history included, constipation, hydronephrosis, hysterosalpingo-oophorectomy, lymphadenectomy in right iliac region, hysterectomy, peritoneal nodule resection, hemicolectomy, ureterectomy, right salpingectomy, and pelvic venous thrombosis. At Screening, tumor assessments of target/non-target lesions via CT scan showed bladder mass, left iliac abdominal and pelvic adenopathy and mesenteric abdominal. The subject received previous radiotherapy to left pelvic bone lesion and left iliac abdominal and pelvic adenopathy. Previous anticancer therapy included doxorubicin, gemcitabine, ifosfamide and docetaxel. Prior and concomitant medications included filgrastim, fluconazole, lactulose, rosuvastatin and warfarin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 16), the subject was hospitalized for intestinal obstruction (Grade 2) due to peritoneal metastasis. She was treated with sodium chloride. On [redacted] (Day 22), the subject recovered from intestinal obstruction. The Investigator considered intestinal obstruction serious and not related to the study drug. The study drug dose was not changed.

On [redacted] (Day 43), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 36).

被験者番号	23021001
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	前庭神経炎/Vestibular neuronitis

A 55-year-old white male was diagnosed with intermediate grade leiomyosarcoma of the bones and joints in the left distal femur on 06 Nov 2006. The last date of disease progression was 01 Jul 2011. Medical history included back pain and fatigue. At Screening, tumor assessments of target/non-target lesions via CT scan showed left upper lobe and right middle lobe lung masses, left medial/quadrate and right lower lobe liver masses, lesions in Th3 and Th12 dorsal vertebral, L5 lumbar and right hilar thoracic adenopathy. The subject received previous radiotherapy to Th 2-4, Th11, Th12 and L1 vertebral lesions and corpus L5 bone lesion. Previous anticancer therapy included angio embolisation with doxorubicin, and trabectedin. Prior and Concomitant medications included alendronic acid, dexamethasone, diclofenac, meroken nadroparin, omeprazole, ondansetron and paracetamol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 35), the subject was diagnosed with deep vein thrombosis (Grade 2) and was treated nadroparin. The subject started feeling nausea and dizziness after getting up. On [redacted] (Day 39), the subject started vomiting (Grade 2) and complained of increasing nausea and dizziness. On [redacted] (Day 41), the subject was hospitalized for further evaluation. A neurological examination was unremarkable except for third degree nystagmus with rapid phase towards the right and mild facial asymmetry to the disadvantage of the left. The subject was diagnosed with vestibular neuronitis (Grade 3). On [redacted] (Day 42), the subject recovered from vomiting. On [redacted] (Day 43), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 26). On [redacted] (Day 110), the subject recovered from vestibular neuroritis and did not recover from DVT. The Investigator considered vestibular neuronitis serious and not related to the study drug; vomiting non-serious and not related to study drug; DVT non-serious and possibly related to study drug.

被験者番号	23021002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	各種物質毒性/Toxicity to various agents

A 48-year-old white female was diagnosed with high grade leiomyosarcoma in the bones and joints of the left femur on 09 Nov 2006. The last date of disease progression was 14 Mar 2012. Significant medical history included excision metastasis in right and left upper lobe lung, osteosynthesis in left proximal humerus, upper abdominal pain, hysterectomy and resection of the tumor distal to column of left femur. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower and left upper lobe lung masses, pancreatic mass, lesions in right 5th rib, right sacrum and right proximal femur. The subject received previous radiotherapy to left arm/hand and right leg/foot and right sacrum. Previous anticancer therapy included doxorubicin, docetaxel, gemcitabine and trabectedin. Prior and Concomitant medications included acenocoumarol, ciprofloxacin, dexamethasone, fentanyl, filgrastim, gabapentin, morphine, nadroparin, ondansetron, oxycodone and paracetamol.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15) the subject experienced decreased white blood cell count (Grade 2) and decreased platelet count (Grade 3) with WBC count 2.5 x 10^9/L (NR: 3.7-11) and platelet count 30 X 10^9/L (NR: 125 – 375). On [redacted] (Day 22) her decreased white blood cell count worsened to Grade 3 with WBC count 1.5 x 10^9/L. On [redacted] (Day 29), the study drug dose was reduced to 750 mg/m^2 due to decreased WBC count. The subject recovered from decreased WBC count on [redacted] (Day 77) and from decreased platelet on [redacted] (Day 29). The Investigator considered decreased WBC count and decreased platelet count non-serious and probably related to the study drug.

On [redacted] (Day 44), the subject experienced decreased platelet count (Grade 3) and the study drug was interrupted and resumed at reduced dose of 600 mg/m^2. She recovered on [redacted] (Day 57). The Investigator considered decreased platelet count non-serious and probably related to the study drug.

On [redacted] (Day 78), the subject experienced decreased platelet count (Grade 1) and the study drug was interrupted. She recovered on [redacted] (Day 85). On the same day, the study drug dose was reduced at 500 mg/m^2. The Investigator considered decreased platelet count non-serious and probably related to the study drug.

On [redacted] (Day 85), the subject received increased fentanyl dose for consistent pain and the following day the subject experienced nausea, vomiting and headache. The subject persistently felt increasing nausea, vomiting and headache and was taken to the emergency due to these events. After examination, subject was found to have fentanyl intoxication (Grade 2) and fentanyl dose was reduced. The subject recovered from this event on [redacted] (Day 91). The Investigator considered this event serious (important medical event) and not related to the study drug.

On [redacted] (Day 106), the subject experienced decreased platelet count (Grade 1) with platelet count of 80 x 10^9/L and the study drug was interrupted. She recovered on [redacted] (Day 113). On the same day, the study drug dose was reduced at 400 mg/m^2. The Investigator considered decreased platelet count non-serious and probably related to the study drug.

On [redacted] (Day 134), the subject experienced decreased platelet count (Grade 2) with platelet count 82 x 10^9/L and the study drug was interrupted. She recovered on [redacted] (Day 141). On the same day, the study drug dose was reduced at 300 mg/m^2. The Investigator considered decreased platelet count non-serious and probably related to the study drug.

On [redacted] (Day 295), subject was withdrawn from the study due to clinical disease progression and the last dose of the study drug was received on [redacted] (Day 274).

被験者番号	24011002
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anaemia，呼吸不全/Respiratory failure，気道感染/Respiratory tract infection

A 61-year-old white female was diagnosed with high grade adipocytic myxoid sarcoma in the connective and soft tissue of the right lower limb in Sept 1999. The last date of disease progression was 24 Oct 2011. Significant medical history included leg amputation (right lower extremity), spinal fusion surgery, spinal laminectomy, back pain and laparotomy. At Screening, tumor assessments of target/non-target lesions via CT scan showed lesions in the lower right lobe of the lung, right iliac fossa, pouch of douglas, and other lung adenopathy. The subject received previous radiotherapy to lumbar spine proximal sacral and thoracic vertebra and previous anticancer therapy included doxorubicin, epirubicin, gemcitabine, ifosfamide, investigational drug and trabectedin. Prior and Concomitant medications included augmentin, fentanyl, filgrastim, loperamide, lorazepam, nystatin, omeprazole, potassium ascorbate, prednisone, tiotropium, trazodone, and venlafaxine. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 45), the subject experienced respiratory tract infection (Grade 2) and she was treated with augmentin and clarithromycin. She recovered from this event on [redacted] (Day 49). The investigator considered respiratory tract infection non-serious and not related to the study drug. On the same day (Day 49), the subject presented to the emergency room and on clinical examination showed respiratory failure (Grade 3), with oxygen saturation of 76% associated with dyspnea (Grade 2), somnolence (Grade 1) and bradyphrenia (Grade 1). The subject was hospitalized for further observation and auscultation of the chest showed significant hypoventilation with severe bronchospasm. Her treatment included acetylcystiene, methylprednisolone, fluconazole, furosemide, and oxygen therapy. On [redacted] (Day 51), X-ray of the thorax revealed increased density at the right base. The study drug was interrupted due to respiratory failure. The subject recovered from somnolence and bradyphrenia on [redacted] (Day 61), from respiratory failure on [redacted] (Day 63) and from dyspnea on [redacted] (Day 100). The Investigator considered respiratory failure serious and not related to the study drug; dyspnea, somnolence, and bradyphrenia non-serious and not related to the study drug. The study drug dose was resumed on [redacted] (Day 76).

On [redacted] (Day 95), the subject was hospitalized due to respiratory tract infection (Grade 3), associated with cough, expectoration, fever, asthenia and general discomfort, and it was determined that she has hypokalemia (Grade 4). Her potassium level on [redacted] (Day 76) was 2.5 mmol/L (NR: 3.5-5). Her treatment included levofloxacin, fluconazole, methylprednisolone, budesonide, ipratropium, and oxygen therapy. The study drug was interrupted due to respiratory tract infection. During her hospitalization on [redacted] (Day 97), the subject experienced anemia (Grade 3), with hemoglobin of 6.0 g/dL (NR: 10.0 – 15.5) and hematocrit of 19.0 % (NR: 33-47). She received three units of red blood cells. The subject recovered from hypokalemia on [redacted] (Day 95) with repeat potassium level of 4.5 mmol/L. She recovered from anemia on [redacted] (Day 98) with repeat hemoglobin of 11.0 g/dL and hematocrit of 32.9% and recovered from respiratory tract infection on [redacted] (Day 100). The Investigator considered anemia and respiratory tract infection serious and not related to the study drug, hypokalemia non-serious and not related to the study drug.

On [redacted] (Day 121), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 113).

On [redacted] (Day 476, 367 days after the last dose), the subject died due to disease progression.

被験者番号	24031004
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腹痛/Abdominal pain、無力症/Asthenia

A 64-year-old white female was diagnosed with high grade leiomyosarcoma in uterus on 15 Nov 2005. The last date of disease progression was 16 Nov 2012. Significant medical history included abdominal pain, anorexia, bilateral salpingo-oophorectomy, appendicetomy, hypercholesterolemia, congestive cardiac failure, spinal osteoarthritis and total hysterectomy. At Screening, tumor assessments of target/non-target lesions via l CT scan showed lesions in liver, trachea/bronchus, retroperitoneal mass and pelvis. The subject received previous radiotherapy to pelvis. Previous anticancer therapy included doxorubicin, ridaforolimus or placebo (investigational drug) and trabectedin. Prior and concomitant medications included amoxi-clavulanic, atorvastatin, bemiparin, carvedilol, contact laxatives, dexamethasone, diazepam, enalapril, lactulose, lorazepam, metoclopramide, midazolam, omeprazole, ondansetron, paroxetine, sodium phosphate monobasic and spironolactone. ECOG performance status at screening was 1. On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 1), the subject started experiencing abdominal pain (Grade 1). On [redacted] (Day 2), the subject started experiencing asthenia (Grade 1) and constipation (Grade 1). On [redacted] (Day 17), the subject was hospitalized for worsening abdominal pain (Grade 3) and worsening asthenia (Grade 3). During hospitalization, the subject experienced jaundice (Grade 3), nausea (Grade 2), vomiting (Grade 2) and worsening constipation (Grade 3). Laboratory results showed AST 45 IU/L (NR: 10-36); ALT 49 IU/L (NR: 10-33), hemoglobin 90 g/L (NR: 110-155) and alkaline phosphatase 271 IU/L (NR: 30-115). The subject was treated with morphine, dexamethasone, metoclopramide, lactulose and paracetamol. The subject did not recover from abdominal pain, constipation and asthenia. On [redacted] (Day 36), the subject recovered from nausea. On [redacted] (Day 37), the event of jaundice improved to Grade 1. The Investigator considered abdominal pain, asthenia serious and not related to the study drug; constipation non-serious and possibly related to study drug jaundice, nausea, non-serious and not related to the study drug.

On [redacted] (Day 39), the subject experienced intestinal obstruction (Grade 2) and liver failure (Grade 3) due to disease progression. The subject was withdrawn from the study due to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 1). Treatment included metoclopramide, morphine, lactulose and paracetamol. On [redacted] (Day 40), the subject recovered from vomiting. The subject did not recover from intestinal obstruction and liver failure. The Investigator considered these events non-serious and not related to the study drug.

被験者番号	24051005
投与群	ダカルバジン群：1200 mg/ m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	肺塞栓症/Pulmonary embolism

A 65-year-old white male was diagnosed with high grade leiomyosarcoma of the connective and soft tissue in the left thigh on 08 Feb 2012. The last date of disease progression was 03 Dec 2012. Significant medical history included epilepsy, left inguinal lymphadenopathy, left pleural effusion, pneumonia and sarcoma excision. At Screening, tumor assessments of target/non-target lesions via CT scan showed right upper lobe and left lower lobe lung masses, multiple lung nodules and multiple pleural nodules. The subject received previous radiotherapy to soft tissue of the extremity and previous anticancer therapy included doxorubicin, ifosfamide, ifosfamide HD and trabectedin. Prior and Concomitant medications included augmentin, dexamethasone, gabapentin, granisetron, iron, paracetamol and prednisone. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 37), the subject started experiencing occasional hemoptysis (Grade 1). On [redacted] (Day 42), the subject experienced dyspnea (Grade 1), cough (Grade 1) and pancytopenia (Grade 2). Tumor response assessment showed disease progression, right pleural effusion and pulmonary embolism. The subject was hospitalized for pulmonary embolism (Grade 3) and pleural effusion (Grade 1). The subject was treated with tinzaparin, prednisone and iron infusion. On [redacted] (Day 49), the subject recovered from pulmonary embolism. On [redacted] (Day 58), the subject recovered from dyspnea and pancytopenia and did not recover from hemoptysis, pleural effusion, cough and dyspnea. The Investigator considered pulmonary embolism serious and not related to the study drug; pleural effusion, cough, hemoptysis, pleural effusion, dyspnea non-serious and not related to the study drug; pancytopenia non-serious and possibly related to study drug.

被験者番号	24071001
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	出血性胃腸潰瘍/Gastrointestinal ulcer haemorrhage

A 53-year-old white male was diagnosed with high grade leiomyosarcoma in the splenic flexure of the large intestine on 21 Aug 2009. The last date of disease progression was 16 Jul 2012. Significant medical history included alcohol use, anorexia, decreased appetite, barrett's oesophagus, diarrhea, colectomy, hepatectomy, tobacco user, cholecystectomy, and neurotoxicity of hands and feet. At Screening, tumor assessments of target/non-target lesions via CT scan showed superior lingual nodule thoracic adenopathy and right middle lobe thoracic adenopathy. Previous anticancer therapy included epirubicin, ifosfamide, paclitaxel, and gemcitabine. Prior and Concomitant medications included acetylsalicylic acid, alprazolam, analgesics, azithromycin, ciprofloxacin, cyanocobalamin, dalteparin, dexamethasone, escitalopram, esomeprazole, iron, metamizole, ondansetron, and paracetamol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 88), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 78).

On [redacted] (Day 98), the subject experienced anemia (Grade 3) with hemoglobin of 76 g/L (NR: 125-170) and hematocrit of 0.299 L/L (NR: 0.37-0.51 L/L). On [redacted] (Day 100), the subject was hospitalized due to gastrointestinal ulcer hemorrhage related to the sarcoma (Grade 3). He was transfused with 5 units of red blood cells. Fibrogastroscopy, gastric biopsy and colonoscopy were performed. All three procedures revealed tumor infiltration due to tumor progression. On [redacted] (Day 103), the subject recovered from gastrointestinal hemorrhage and recovered from anemia on [redacted] (Day 175). The Investigator considered gastrointestinal ulcer hemorrhage serious and not related to the study drug but secondary to tumor infiltration; anemia non-serious and not related to the study drug.

被験者番号	26011006
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腸閉塞/Intestinal obstruction，好中球減少症/Neutropenia，血小板減少症/Thrombocytopenia

A 51-year-old white male was diagnosed with high grade adipocytic myxoid sarcoma in retroperitoneum on Dec 2006. The last date of disease progression was Dec 2012. Significant medical history included hemi-cholectomy, cholecystectomy, nephrectomy, abdominal discomfort, and cholecystitis. At Screening, tumor assessments of target/non-target lesions via CT scan showed central, upper and lower right abdomen masses and bladder lesions. Previous anticancer therapy included trabectedin, gemcitabine, docetaxel and doxorubicin. Concomitant medications included domperidone, electrolytes w/macrogol, hyoscine, paracetamol, piperacillin/tazobactam, and sennoside. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 20), the subject was hospitalized for thrombocytopenia (Grade 4), worsening neutropenia (Grade 4), intestinal obstruction (Grade 3), and abdominal pain (Grade 3). Laboratory results showed platelets count 13 x10^9/L (NR: 125-375), white blood cell (WBC) count 0.9 x10^9/L (NR: 3.7-11) and neutrophil count 0.16 x 10^9/L (NR: 1.7 – 7.9). The study drug was interrupted due to these events. The subject was treated with docusate, dexamethasone, lansoprazole, panadeine, sennoside, magrogol and morphine, filgramstim, platelets and carbohydrates with fat and nutrients.On [redacted] (Day 24), the subject recovered from bowel obstruction. He recovered with sequelae from neutropenia and thrombocytopenia on [redacted] (Day 29), The subject did not recover from constipation and abdominal pain. The Investigator considered intestinal obstruction serious and not related to study drug; constipation, abdominal pain non-serious and not related to study drug; neutropenia, thrombocytopenia non-serious and probably related to study drug.

On [redacted] (Day 34), the subject was hospitalized due to intestinal obstruction (Grade 3). He underwent CT scan of the abdomen which showed incomplete obstruction of the residual colon. The study drug was withdrawn due to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 1). Treatment included docusate, lansoprazole, panadeine, morphine and dietary supplement., On [redacted] (Day 43), the subject recovered with sequelae from intestinal obstruction. The Investigator considered this event serious and not related to study drug. The subject died on [redacted] (Day 64, 63 days after last dose) due to disease progression.

被験者番号	26011007
投与群	ダカルバジン群：1200 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	白血球減少症/Leukopenia，好中球減少症/Neutropenia，血小板減少症/Thrombocytopenia
治験薬の投与中止に至った有害事象	血小板減少症/Thrombocytopenia

A 56-year-old white female was diagnosed with high grade leiomyosarcoma of the inferior vena cava on 14 Jun 2006. The last date of disease progression was 07 Mar 2013. Significant medical history included thoracotomy, metastectomy, and surgical resection of leiomyosarcoma encasing the inferior vena cava. At Screening, tumor assessments of target/non-target lesions via CT scan showed left upper lobe lung mass, parahiliar left lung mass, segment II liver mass, pancreatic mass, and lesions in right pelvis and throughout lung. The subject received previous radiotherapy to abdominal and pelvic adenopathy para-caval and T3-T5. Previous anticancer therapy included axitinib and doxorubicin. Prior and concomitant medications included amlodipine, gentamicin, meropenem, paracetamol and propranolol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 13), the subject experienced leukopenia (Grade 4) and neutropenia (Grade 4). Laboratory results showed white blood cell (WBC) count of 0.7 x 10^9/L (NR: 3.7-11) and neutrophil count of 0.24 x 10^9/L (NR: 1.7 –7.9) and the study drug was interrupted due to leukopenia. The subject was treated with piperacillin/tazobactam. She recovered from leukopenia on [redacted] (Day 42) and from neutropenia on [redacted] (Day 43). The Investigator considered neutropenia, leukopenia serious and probably related to the study drug.

On [redacted] (Day 16), the subject was hospitalized for thrombocytopenia (Grade 3), anemia (Grade 2) and an unknown infection (Grade 3) with platelet counts 33 x10^9/L (NR: 125-375) . The study drug was interrupted due to infection. She was treated with filgrastim, red blood cell transfusion, gentamicin, meropenem and platelets. On [redacted] (Day 21), the subject recovered from anemia; recovered from infection on [redacted] (Day 28) and from thrombocytopenia on [redacted] (Day 43). The subject was withdrawn from study due to thrombocytopenia and received the last dose of the study drug on [redacted] (Day 1). The Investigator considered thrombocytopenia serious and probably related to study drug; unknown infection non-serious and probably related to study drug; and anemia non-serious and possibly related to study drug,

被験者番号	26021005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	非心臓性胸痛/Non-cardiac chest pain
病勢進行による死亡	Yes

A 58-year-old white male was diagnosed with high adipocytic dedifferentiated in testis on 21 Sep 2010. The last date of disease progression was 09 Oct 2012. Significant medical history included crohns disease, left hemi-scrotectomy, left orchidectomy, pulmonary embolus, and non-cardiac chest pain. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lower lobe lung mass, subcutaneous mass in left shoulder blade and multiple lung metastases. Previous anticancer therapy included doxorubicin, ifosphamide and trabectidin. Prior and concomitant medications included amitriptyline, amoxicillin, clonazepam, dalteparin, gabapentin, haloperidol, lekovit ca, loperamide, morphine, omeprazole, paracetamol, prednisolone, sulfasalazine and zopiclone. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 22), the subject experienced thrombocytopenia (Grade 3) with platelet count of 47 x10^9/L (NR: 125-375). The event of thrombocytopenia did not resolve. The study drug was interrupted due to this event. On [redacted] (Day 24), the subject was hospitalized due to non-cardiac chest pain (Grade 3) and was treated with morphine, and piperacillin/tazobactam. The event of non-cardiac chest pain did not resolve. The Investigator considered thrombocytopenia non-serious and probably related to the study drug; non-cardiac chest pain serious and possibly related to the study drug.

On [redacted] (Day 25, 24 days after last dose), the subject died due to clinical disease progression. The subject received the last dose of the study drug on [redacted] (Day 1).

被験者番号	32011001
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	肺転移/Metastases to lung, 好中球減少症/Neutropenia

A 43-year-old asian female was diagnosed with high grade leiomyosarcoma in retroperitoneum on 11 Oct 2007. The last date of disease progression was 16 Sep 2011. Significant medical history included benign neoplasm of thyroid gland, peritoneal tumor excision, hepatectomy, partial lung resection, and peripheral sensory neuropathy. At Screening, tumor assessments of target/non-target lesions via CT scan showed right lower lobe lung mass, left lingular lobe lung mass, and multiple pulmonary nodules. Previous anticancer therapy included docetaxel, epirubicin, gemcitabine, and ifosfamide. Prior and Concomitant medications included augmentin, azithromycin, dexamethasone, lorazepam, metoclopramide, ondansetron, paracetamol, and sennoside. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 11), the subject experienced white blood cell count decreased (Grade 1), with WBC count of 3.5 x10^9/L (NR: 3.7-11). On [redacted] (Day 22), the event worsened to Grade 2 associated with neutropenia (Grade 3) with WBC count of 2.03 x 10^9/L and neutrophil count of 0.57 x10^9/L (NR: 1.7-7.9). The subject recovered from both events on [redacted] (Day 29). The Investigator considered white blood cell count decreased non-serious and possibly related to the study drug; neutropenia serious (medically important event) and possibly related to the study drug. On the same day (Day 29) the subject again experienced white blood count decreased (Grade 1) and neutropenia (Grade 2) with WBC count of 3.29 x 10^9/L and neutrophil count of 1.06 x 10^9/L. The subject recovered from both events on [redacted] (Day 35) with WBC counts 5.8 x10^9/L and neutrophil counts 3.5 x10^9/L. The Investigator considered both events non-serious and possibly related to the study drug.

On [redacted] (Day 123), the subject was hospitalized due to metastasis to lung (Grade 3). Tumor response assessment on the same day showed disease progression and the subject was withdrawn from the study. The subject received the last dose of the study drug on [redacted] (Day 99). On [redacted] (Day 132*), the subject underwent left thoracotomy with left lower lobectomy with wedge resection of lingular lobe with pariectal pericardectomy. Treatment included pregabalin, omeprazole, digoxin, tramadol, paracetamol and prednisolone. The subject did not recover from this event. The Investigator considered metastasis to lung serious and not related to the study.

* 新薬承認情報提供時に置き換え

被験者番号	33011004
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	呼吸困難/Dyspnoea
病勢進行による死亡	Yes

A 53-year-old asian female was diagnosed with intermediate grade leiomyosarcoma in ovary and right ovarian vein on 06 Apr 2011. The last date of disease progression was 12 Dec 2012. Significant medical history included right gonadal vein thrombosis, spondylolisthesis, pulmonary hemorrhage, cough, enterobacter bacteraemia, hypotension, left lung biopsy and lung infection. At Screening, tumor assessments of target/non-target lesions via CT scan showed right and left upper lobe lung mass and lesions in right ilium. Previous anticancer therapy included ifosfamide, trabectedin and doxorubicin. Prior and concomitant medications included acetylcysteine, amoxicillin with clavulanate potassium, azithromycin, cefepime, ceftriaxone, ciprofloxacin, codeine, codipront, dexamethasone, dextromethorphan, gelatin, granisetron, lactulose, meropenem, paracetamol, piperacillin/tazobactam, promethazine w/codeine, red blood cells, sennoside a+b, sodium chloride, tranexamic acid and vancomycin. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 36), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 22).

On [redacted] (Day 39), the subject was hospitalized for dyspnea (Grade 4) associated with right pleuritic chest pain, tachypnea and oxygen saturation of 83%. Chest X ray revealed multiple disseminated bilateral lung nodules in both lung fields, cardiac margins were obscured by the bilateral lung nodules. The subject was treated with morphine, oxygen, fentanyl, hydrocortisone and hyoscine. On [redacted] (Day 42, 20 days after last dose), the subject died due to disease progression. The Investigator considered dyspnea serious and not related to the study drug, but related to disease progression.

被験者番号	35011005
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	悪性腹水/Malignant ascites

A 49-year-old asian male was diagnosed with high grade leiomyosarcoma in ano-rectum (sigmoid colon) on 15 Sep 2011. The last date of disease progression was 19 Mar 2013. Significant medical history included sigmoidectomy, behcet's syndrome, colon biopsy, peripheral edema, pneumonia fungal, pleural effusion, and pericardial effusion. At Screening, tumor assessments of target/non-target lesions via CT scan showed peritoneal seeding nodule, bilateral pleural effusion and pericardial effusion. Previous anticancer therapy included doxorubicin, docetaxel, gemcitabine, and ifosfamide. Prior and Concomitant medications included albumin human, amiloride, amino acids w/calcium/glucose/magnesium/p, aprepitant, calcium polystyrene sulfonate, dexamethasone, furosemide, heparin, hydrocortisone, lactulose, multitrace-4, myprodol, paracetamol, pethidine, prednisolone, ramosetron, sodium bicarbonate, sodium carbonate anhydrous, tramadol, ultracet and vitamins. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 16), the subject was hospitalized due to malignant ascites (Grade 3). On [redacted] (Day 20), tumor response assessment showed disease progression and the subject was withdrawn from the study. The subject received last dose of the study drug on [redacted] (Day1). On [redacted] (Day 21), he underwent ascites catheter insertion. The subject recovered from this event on [redacted] (Day 27). The Investigator considered malignant ascites serious and not related to the study drug.

被験者番号	35031001
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	神経痛/Neuralgia

A 64-year-old asian female was diagnosed with high grade leiomyosarcoma in lung and bronchus on 21 Dec 2007. The last date of disease progression was 10 Nov 2011. Medical history included diabetes mellitus, cholelithiasis, hypertension, hypothyroidism, tumor excision, peripheral sensory neuropathy, back pain and hyperlipidaemia. At Screening, tumor assessments of target/non-target lesions via CT-scan showed lesions to T11 vertebral body. The subject received previous radiotherapy to sternal lesion and mediastinum. Previous anticancer therapy included dacarbazine, doxorubicin, ifosfamide, docetaxel and gemcitabine. Prior and concomitant medications included acetylcysteine, alanyl glutamine, albumin human, alendronic acid, amino acids, aminomethylbenzoic acid, aprepitant, atorvastatin, bromhexine, calcium carbonate, ceftezole, ciprofloxacin, citrulline, cyanocobalamin, diphenylpyraline, etizolam, eupatilin, famotidine, fluconazole, gabexate, general nutrients, insulin, insulin glulisine, iron, lactitol, levothyroxine, lidocaine, losartan, magnesium, magnesium hydroxide, metoclopramide, midazolam, multiblue5, myprodol, nicardipine, palonosetron, phytomenadione, propacetamol, ramosetron, ranitidine, simeticone, solutions for parenteral nutrition, triamcinolone, ulinastatin, unspecified herbal and traditional medicine, vancomycin, vitamin k , vitamins and zinc . At Screening, peripheral neuropathy was Grade 1 and ECOG performance status was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 78), the subject was hospitalized due to neuralgia (Grade 3) and treated with dexamethasone, morphine, oxycodone, freamine, fentanyl and pregabalin. During hospitalization, she underwent facet joint block and DRG block bilateral L3 and L2. She recovered from neuropathic pain on [redacted] (Day 94). The subject did not recover from myalgia. The Investigator considered neuralgia serious and not related to the study drug

On [redacted] (Day 103) the subject was hospitalized for recurrence of neuralgia (Grade 3). The subject was also found to have left lower extremity weakness (Grade 3) and peripheral sensory neuropathy (Grade 2). On [redacted] (Day 108), spine MRI showed probable recurred mass on T11 vertebral body and acute compression fracture of L3 (Grade 3). She was treated with pregabalin, ultracet, morphine and pethidine. During hospitalization, she underwent vertebroplasty L3. On [redacted] (Day 108), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 93). On [redacted] (Day110), the subject recovered from acute compression fracture of L3. On [redacted] (Day 114), the subject underwent corpectomy on T12, IBF (inter body fusion) facet joint block and T11 L1cSynex decompressive laminectomy/foraminotomy. On [redacted] (Day 153), the subject recovered from muscular weakness and peripheral neuropathy. On [redacted] (Day 159), the subject recovered from neuralgia. The Investigator considered neuralgia serious and not related to the study drug; muscular weakness, peripheral sensory neuropathy, acute compression fracture of L3 non-serious and not related to study drug.

被験者番号	41011005
投与群	ダカルバジン群：850 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	好中球減少症/Neutropenia，胸水/Pleural effusion，血小板減少症/Thrombocytopenia
治験薬の投与中止に至った有害事象	血小板減少症/Thrombocytopenia

A 55-year-old white male was diagnosed with high grade liposarcoma in connective and soft tissue of left chest wall on 05 Sep 2006. The last date of disease progression was 11 Jan 2013. Significant medical history included myocardial ischemia, liposarcoma extirpation, coronary metallic stent insertion, pleural effusion, autotransplatation of skin, diabetes mellitus type 2, encephalophathy, hypertension, fasciotomy, pneumonectomy, sepsis, skin necrosis, venous stenosis and venous insuficiency of lower extremity. At Screening, tumor assessments of target/non-target lesions via CT scan showed right upper lobe, middle lobe and lower lobe lung masses. The subject received previous radiotherapy to the chest wall in association with axillary node radiation. Previous anticancer therapy included doxorubicine, ifosphamide, and trabectedin. Prior and concomitant medications included bromazepam, dexamethasone, enoxaparin, fentanyl, granisetron, metamizole, mirtazapine, omeprazole, pamaton, potassium, ranitidine, red blood cells and sodium chloride. ECOG performance status at screening was 2.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 8), the subject was hospitalized for pleural effusion (Grade 2). He underwent thoracocentesis and recovered on [redacted] (Day 11). The Investigator considered pleural effusion serious and not related to the study drug.

On [redacted] (Day 15), the subject was hospitalized for thrombocytopenia (Grade 4) with platelet counts 15 x10^9/L (NR: 125-375). The subject underwent platelet transfusion and the study drug was withdran due to thrombocytopenia. The subject received the last dose of the study drug on 06 Feb 2013 (Day 1). On [redacted] (Day 18), the thrombocytopenia improved to Grade 3 and the subject had neutropenia (Grade 1), anemia (Grade 3) and decreased WBC (Grade 2). On [redacted] (Day 21), the subject recovered from anemia. On [redacted] (Day 24), neutropenia worsened to Grade 4 with neutrophil counts 0.36 x 10^9/L (NR: 1.7 – 7.9) and decreased WBC worsened to Grade 3 with WBC count of 1.53 x10^9/L (NR: 3.7-11). The subject was treated with ciprofloxacin. The subject recovered from thrombocytopenia, neutropenia and decreased white blood cell count on [redacted] (Day 43). The Investigator considered thrombocytopenia, neutropenia serious and probably related to the study drug; anemia, WBC decreased non-serious and probably related to study drug.

On [redacted] (Day 51), the tumor response assessment showed disease progression. The subject died on [redacted] (Day 88, 87 days after the last dose) due to disease progression.

被験者番号	41021002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	低血圧/Hypotension

A 67-year-old white female was diagnosed with high grade leiomyosarcoma in retroperitoneum on 15 Dec 2009. The last date of disease progression was 10 Dec 2012. Significant medical history included cholelithiasis, type 2 diabetes mellitus, hepatitis A, ankle fracture, hydronephrosis, hypertension, excision of retroperitoneal leiomyosarcoma, nephrectomy and splenectomy. At Screening, tumor assessments of target/non-target lesions viaCT scan showed retroperitoneal mass, small bowel mass and right and left lung masses. Previous anticancer therapy included doxorubicin and trabectedin. Prior and concomitant medications included amlodipine, granisetron, ibuprofen, perindopril and rilmenidine. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 1), the subject was admitted to the hospital experiencing vertigo due to hypotension (Grade 2). Blood pressure was noted as 110/60. During hospitalization, she was hydrated with plasmalyte. On [redacted] (Day 3), hypotension was considered as resolved. The Investigator considered hypotension serious and not related to the study drug.

On [redacted] (Day 22) the subject experienced thrombocytopenia (Grade 3) with platelet counts 32 x 10^9/L (NR: 125 – 375) and the study drug was interrupted due to this event. She recovered from thrombocytopenia on [redacted] (Day 60). On [redacted] (Day 81), the subject experienced thrombocytopenia (Grade 3) with platelet count of 39 x 10^9/L (NR: 125-375). On [redacted] (Day 88), thrombocytopenia improved to grade 1 and was considered resolved on [redacted] (Day 97). On the same day, the study drug dose was reduced to 850 mg/m^2 due to thrombocytopenia. The Investigator considered thrombocytopenia non-serious and possibly related to the study drug.

On [redacted] (Day 124), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 118).

被験者番号	41031002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	末梢性運動ニューロパチー/Peripheral motor neuropathy
治験薬の投与中止に至った有害事象	末梢性運動ニューロパチー/Peripheral motor neuropathy

A 50-year-old white male was diagnosed with intermediate grade leiomyosarcoma in the right supraclavicular site on 30 Apr 2009. The last date of disease progression was 19 Nov 2011. Significant medical history included elevated liver enzymes, hypertension, cancer pain, osteoarthritis, peripheral sensory neuropathy, meningitis, thrombosis in device, tumor excision and knee operation. At Screening, tumor assessments of target/non-target lesions via CT scan showed right middle lobe and left upper lobe lung masses, retroperitoneum, subcaecalis, hypogastrium and caudate lobe of liver mass. The subject received previous radiotherapy to right upper cervical lymphadenopathy. Previous anticancer therapy included docetaxel, gemcitabine, doxorubicin, ifosfamide and trabectedin. Prior and concomitant medications included alprazolam, buprenorphine, diclofenac, essentiale, ginkgo biloba, glycerol, lactulose, metamizole, morphine, nadroparin, omeprazole, ondansetron, paracetamol, perindopril, potassium w/sodium chloride, silybum marianum, tramadol and zolpidem. At Screening, peripheral neuropathy was Grade 1 and ECOG performance status was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 8), the subject was hospitalized with walking difficulties and urinary incontinence (Grade 3). During examination subject found have rubbery legs feeling, lack of control in lower extremities and coldness in legs. The subject underwent MRI of the spine which showed metastases of the vertebra and thoracic spine significantly compressed. He was diagnosed with peripheral motor neuropathy (Grade 3). The study drug was withdrawn. The subject received the last dose of the study drug on [redacted] (Day 1). On the same day, urinary catheter was placed. On [redacted] (Day 9), the subject underwent radiotherapy to Th7-Th12 region. During hospitalization, treatment with dexamethasone and pregabalin was given. On [redacted] (Day 28), the subject recovered from urinary incontinence and neuropathy recovered with sequelae. The Investigator considered peripheral motor neuropathy serious and not related to the study drug; urinary incontinence non-serious and not related to study drug.

被験者番号	46041009
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	腹痛/Abdominal pain，ヘモグロビン減少/Decreased Hemoglobin

A 59-year-old white female was diagnosed with high grade leiomyosarcoma in pancreas on 26 Nov 2010. The last date of disease progression was 15 Nov 2012. Significant medical history included blood alkaline phosphatase increased, gamma-glutamyltransferase increased, hypoalbuminaemia, renal colic, abdominal pain, type 2 diabetes mellitus, hyperlipidaemia, and osteopenia. At Screening, tumor assessments of target/non-target lesions via CT scan showed left lower lobe lung mass, liver mass (segments 7-8), pancreatic mass and single right pelvic bone mass. Previous anticancer therapy included doxorubicin, ifosfamide, trabectedin, pazopanib, gemcitabine, and paclitaxel. Prior and concomitant medications included atorvastatin, dexamethasone, dextrose and sodium chloride injection, escitalopram, insulin glargine, lactulose, lorazepam, metformin, omeprazole, ondansetron, ranitidine, sodium chloride and tramadol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 20), the subject experienced abdominal pain (Grade 2) and was treated with oxycodone. On [redacted] (Day 22), the subject experienced platelet count decreased (Grade 1) with platelet count 108 x 10^9/L (NR: 125 – 375). On [redacted] (Day 29), she recovered from abdominal pain. The Investigator considered abdominal pain non-serious and not related to the study drug.

On [redacted] (Day 36), decreased platelet count worsened to Grade 3 with platelet count of 39 x 10^9/L and on [redacted] (Day 43), it further worsened to grade 4 with platelet count of 25 x 10^9/L. The study drug was interrupted due to decreased platelet count. On [redacted] (Day 50), decreased platelet count improved to Grade 2 and the subject recovered on [redacted] (Day 64). On the same day, the study drug dose was reduced to 750 mg/m^2 due to decreased platelet count. The Investigator considered decreased platelet count non-serious and possibly related to the study drug.

On [redacted] (Day 85) the subject experienced abdominal pain related to disease (Grade 2). On [redacted] (Day 93), the subject was hospitalized for abdominal pain related to disease (Grade 3). She was treated with oxycodone/naloxone, fentanyl and ibuprofen. On [redacted] (Day 97), abdominal pain was recovered. The Investigator considered abdominal pain serious and not related to the study drug.

On [redacted] (Day 141), the subject was hospitalized due to decreased hemoglobin (Grade 3) with hemoglobin of 84 g/L (NR: 110-155). The subject experienced weakness and inability to eat and received blood transfusion on the same day. During hospitalization, the subject was treated with blood transfusion. On [redacted] (Day 152), she recovered from decreased hemoglobin. The Investigator considered decreased hemoglobin serious and not related to the study drug.

On [redacted] (Day 149), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 127).

被験者番号	48081001
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	病的骨折/Pathological fracture

A 52-year-old white male was diagnosed with intermediate grade leiomyosarcoma in retroperitoneum on 22 Sep 2005. The last date of disease progression was 23 Feb 2013. Significant medical history included depression, pain in extremity, lung neoplasm surgery, resection of retroperitoneal tumor, and subcutaneous nodule (chest wall and right leg). At Screening, tumor assessments of target/non-target lesions via CT scan showed left quadrate lobe liver mass, pleural mass, single lesion in right leg/foot bone, left lingular lobe lung mass, left lower lobe lung mass and splenic mass. The subject received previous radiotherapy to right femur bone. Previous anticancer therapy included ifosfamide and doxorubicin. Prior and concomitant medications included amitriptyline, atropine, bromopride, bupivacaine w/glucose, captopril, cefazolin, ciprofloxacin, clonazepam, dexamethasone, diazepam, enoxaparin, esmolol, etilefrine, etomidate, fentanyl, flebobag ring lact, fluconazole, furosemide, glucose, haloperidol, heparin, hydrocortisone, insulin, ipratropium, lactulose, lidocaine, linezolid, meropenem, metamizole, metoclopramide, midazolam, morphine, nalbuphine, neostigmine, norepinephrine, omeprazole, ondansetron, oxacillin, pancuronium, phenylephrine, polymyxin b, potassium, propofol, ranitidine, red blood cells, rivaroxaban, ropivacaine, sodium chloride, tandrilax, terbutaline, tigecycline, and tramadol. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 39), tumor response assessment showed disease progression and the subject was withdrawn from the study. The last dose of the study drug was received on [redacted] (Day 23).

On [redacted] (Day 46), the subject was hospitalized due to pathological fracture of the femur (Grade 4) at the site of metastasis. A right thigh X-ray showed pathologic fracture of the transtrochanteric area. He underwent surgical treatment of right proximal femur. On [redacted] (Day 53), the subject was discharged from the hospital. On [redacted] (Day 67), the subject was re-hospitalized for failure of intramedullary femur rod (Grade 4) with the intention for re-surgery. On [redacted] (Day 72), the subject underwent removal of material synthesis, surgical wound debridement and resection of bone tumor endoprosthesis replacement. Per the hospital report, the debridement that occurred was due to the surgical wound infection. On [redacted] (Day 77), the subject was transferred to ICU and experienced surgical wound infection, urinary tract infection and underwent tracheostomy for mechanical ventilation. He did not recover from pathological fracture of the femur and failure of intramedullary femur rod. On [redacted] (Day 93, 70 days after the last dose), the subject died due to multi-organ failure secondary to sepsis. The Investigator considered pathological fracture and failure of intramedullary femur rod serious and not related to the study drug.

被験者番号	48091008
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	薬物過敏症/Drug hypersensitivity
治験薬の投与中止に至った有害事象	薬物過敏症/Drug hypersensitivity

A 35-year-old white female was diagnosed with intermediate grade leiomyosarcoma in uterus on 30 Nov 2010. The last date of disease progression was 23 Oct 2012. Significant medical history included peripheral edema, pain in extremity and systemic arterial hypertension. At Screening, tumor assessments of target/non-target lesions via CT scan showed pre-vascular mediastinal chain thoracic lymphadenopathy, right abdominal and pelvic iliac lymphadenopathy, right inguinal lymphadenopathy, left upper lobe lung mass, right lower lobe lung mass, between pancreas tail mass and splenic hilum, left pelvic cavity in contact with the sigmoid colon and bladder side wall, colorectal mass, ischiorectal fossa in touch with the right lateral of the rectum and the elevator anus muscle, right and left hilar thoracic lymphadenopathy. The subject received previous radiotherapy to pelvis. Previous anticancer therapy included docetaxel, gemcitabine, doxorubicin, and ifosfamide. Prior and concomitant medications included ciprofloxacin, dexamethasone, furosemide, losartan, morphine, ondansetron and panadeine. ECOG performance status at screening was 1.

On [redacted] (Day 1), treatment with study drug was initiated. During study drug infusion, the subject experienced drug hypersensitivity (Grade 3), with symptoms including chills and tremors. He was treated with dexamethasone and metamizole and recovered from this event on the same day. The Investigator considered this event serious and probably related to the study drug.

On [redacted] (Day 21), the subject experienced drug hypersensitivity (Grade 3) during study drug infusion, with symptoms including fever, pain in the left thigh, chills and mild dyspnea. The study drug was withdrawn due to this event and the subject received the last dose of the study drug on the same day. The subject was treated with hydrocortisone and metamizole and recovered on the same day. The subject was withdrawn from the study due to this event. The Investigator considered this event serious and probably related to the study drug.

被験者番号	48111002
投与群	ダカルバジン群：1000 mg/m^2 IV on Day 1, every 21 days
死亡以外の重篤な有害事象	貧血/Anaemia，深部静脈血栓症/Deep vein thrombosis，発熱性好中球減少症/Febrile neutropenia，腸出血/Intestinal haemorrhage，血小板減少症/Thrombocytopenia，尿路感染/Urinary tract infection

A 68-year-old white male was diagnosed with high grade adipocytic dedifferentiated in retroperitoneum on 22 Jan 2009. The last date of disease progression was 03 Sep 2012. Medical history included diabetes mellitus, hypothyroidism, explorative laparotomy, lymphadenectomy, aortic valve incompetence, and tumor excision. At Screening, tumor assessments of target/non-target lesions via spiral CT scan showed soft tissue mass in ileo-psoas and left psoas, and lesions in left inguinal abdominal and pelvic adenopathy. The subject received previous radiotherapy to musculoskeletal - soft tissue left flank. Previous anticancer therapy included AVE8062/placebo, paclitaxel, cisplatin, docetaxel, gemcitabine, doxorubicin and ifosfamide. Prior and concomitant medications included aminocaproic acid, bromopride, calcium carbonate with vitamin d, calcium gluconate, citalopram, clonazepam, coloxyl with danthron, dimeticone, diphenhydramine, domperidone, erythrocytes, glycerol, insulin, levothyroxine, lorazepam, metamizole, minerals with vitamins, ondansetron, potassium, tramadol, trimebutine, vildagliptin, and vitamin k. ECOG performance status at screening was 0.

On [redacted] (Day 1), treatment with study drug was initiated.

On [redacted] (Day 15), the subject was hospitalized due to urinary tract infection (Grade 3) and treated with ciprofloxacin. He recovered from this event on [redacted] (Day 26). The Investigator considered urinary tract infection serious and not related to the study drug.

On [redacted] (Day 19) he experienced anemia (Grade 3) and intestinal hemorrhage (Grade 2). On [redacted] (Day 20), the subject was hospitalized for anemia (Grade 4), thrombocytopenia (Grade 4) with and intestinal hemorrhage (Grade 3). Laboratory results showed hemoglobin level of 56 g/L (NR: 125 – 170), hematocrit of 17% (NR: 37 – 51) and platelet counts 7 x 10^9/L (NR: 125 – 375). The study drug was interrupted due to intestinal hemorrhage. He was treated with intravenous tranexamic acid, omeprazole, vitamin K and dipyrone. He also received platelet transfusion, erythrocyte transfusion, diphenhydramine and hydrocortisone. On [redacted] (Day 24), the subject developed deep venous thrombosis (Grade 3) related to his bedridden condition and was treated with enoxaparin, warfarin, calcium gluconate, and potassium chloride. On [redacted] (Day 26), the subject experienced febrile neutropenia (Grade 3) and was treated with cefepime, vancomycin, paracetamol, hydrocortisone, pethidine, and furosemide. He recovered from anemia on [redacted] (Day 27), from intestinal hemorrhage on [redacted] (Day 35) from thrombocytopenia on [redacted] (Day 30) and from febrile neutropenia on [redacted] (Day 35). He did not recover from deep vein thrombosis. The Investigator considered anemia, thrombocytopenia and febrile neutropenia serious and probably related to the study drug; deep venous thrombosis serious and not related to the study drug; intestinal hemorrhage non-serious and not related to the study drug. The study drug remained interrupted.

On [redacted] (Day 40) the subject was hospitalized for abdominal pain (Grade 3). On [redacted] (Day 41), he underwent a laparotomy with ileostomy. He was given oxygen and treated with morphine, tramadole, bromide, omeprazole, ranitidine and several antibiotics. He also received red blood cells and plasma transfusions. The Investigator considered abdominal pain serious and not related to the study drug. On [redacted] (Day 42, 41 days from last study drug dose), the subject died due to a neoplastic abdominal pain secondary to clinical disease progression. The last dose of the study drug was received on [redacted] (Day 1).

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any TEAEs	36 (97.3)	20 (54.1)	38 (95.0)	19 (47.5)	19 (100.0)	9 (47.4)	31 (100.0)	18 (58.1)	124 (97.6)	66 (52.0)
血液およびリンパ系障害	3 (8.1)	3 (8.1)	2 (5.0)	2 (5.0)	3 (15.8)	3 (15.8)	3 (9.7)	2 (6.5)	11 (8.7)	10 (7.9)
貧血	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
発熱性好中球減少症	3 (8.1)	3 (8.1)	1 (2.5)	1 (2.5)	3 (15.8)	3 (15.8)	1 (3.2)	1 (3.2)	8 (6.3)	8 (6.3)
リンパ節痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
好中球減少症	0	0	1 (2.5)	1 (2.5)	1 (5.3)	1 (5.3)	0	0	2 (1.6)	2 (1.6)
心臓障害	4 (10.8)	0	2 (5.0)	1 (2.5)	1 (5.3)	0	3 (9.7)	0	10 (7.9)	1 (0.8)
狭心症	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
第一度房室ブロック	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
心不全	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
動悸	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
心嚢液貯留	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
洞性頻脈	4 (10.8)	0	1 (2.5)	0	1 (5.3)	0	0	0	6 (4.7)	0
上室性頻脈	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 15.0.

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付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
耳および迷路障害	2 (5.4)	0	3 (7.5)	0	0	0	2 (6.5)	0	7 (5.5)	0
難聴	0	0	2 (5.0)	0	0	0	0	0	2 (1.6)	0
耳不快感	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
耳出血	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
耳痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
外耳痛	2 (5.4)	0	0	0	0	0	0	0	2 (1.6)	0
眼障害	6 (16.2)	0	2 (5.0)	0	0	0	0	0	8 (6.3)	0
白内障	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
眼乾燥	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
眼痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
流涙増加	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
オキュラーサーフェス疾患	3 (8.1)	0	0	0	0	0	0	0	3 (2.4)	0
霧視	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
胃腸障害	30 (81.1)	5 (13.5)	31 (77.5)	3 (7.5)	15 (78.9)	1 (5.3)	19 (61.3)	2 (6.5)	95 (74.8)	11 (8.7)
腹部癒着	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 15.0.

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付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)										
腹部不快感	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
腹部膨満	4 (10.8)	0	1 (2.5)	0	0	0	0	0	5 (3.9)	0
腹痛	11 (29.7)	0	7 (17.5)	0	4 (21.1)	0	7 (22.6)	1 (3.2)	29 (22.8)	1 (0.8)
上腹部痛	0	0	1 (2.5)	0	1 (5.3)	0	1 (3.2)	0	3 (2.4)	0
裂肛	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
肛門出血	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
肛門直腸静脈瘤出血	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
腹水	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
便秘	6 (16.2)	0	14 (35.0)	2 (5.0)	6 (31.6)	0	8 (25.8)	0	34 (26.8)	2 (1.6)
下痢	9 (24.3)	0	12 (30.0)	0	4 (21.1)	1 (5.3)	5 (16.1)	0	30 (23.6)	1 (0.8)
口内乾燥	1 (2.7)	0	1 (2.5)	0	0	0	3 (9.7)	0	5 (3.9)	0
十二指腸潰瘍	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
消化不良	2 (5.4)	1 (2.7)	8 (20.0)	0	0	0	3 (9.7)	0	13 (10.2)	1 (0.8)
嚥下障害	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
鼓腸	1 (2.7)	0	1 (2.5)	0	0	0	2 (6.5)	0	4 (3.1)	0
排便回数増加	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 15.0.

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付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)										
胃腸管瘻	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
消化器痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
胃食道逆流性疾患	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
胃食道炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
歯肉痛	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
歯肉炎	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
痔核	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
イレウス	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
腸閉塞	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
口腔内出血	0	0	1 (2.5)	0	1 (5.3)	0	1 (3.2)	0	3 (2.4)	0
悪心	16 (43.2)	1 (2.7)	12 (30.0)	0	9 (47.4)	0	8 (25.8)	0	45 (35.4)	1 (0.8)
嚥下痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
食道痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
食道炎	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
口腔内痛	1 (2.7)	0	0	0	1 (5.3)	0	2 (6.5)	0	4 (3.1)	0
歯周病	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 15.0.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)										
直腸分泌物	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
小腸出血	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
口内炎	5 (13.5)	2 (5.4)	9 (22.5)	0	3 (15.8)	0	7 (22.6)	1 (3.2)	24 (18.9)	3 (2.4)
亜イレウス	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
歯痛	0	0	1 (2.5)	0	0	0	1 (3.2)	0	2 (1.6)	0
臍ヘルニア	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
上部消化管出血	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
嘔吐	11 (29.7)	2 (5.4)	7 (17.5)	1 (2.5)	3 (15.8)	0	5 (16.1)	0	26 (20.5)	3 (2.4)
一般・全身障害および投与部位の状態	29 (78.4)	5 (13.5)	35 (87.5)	10 (25.0)	15 (78.9)	3 (15.8)	24 (77.4)	1 (3.2)	103 (81.1)	19 (15.0)
カテーテル留置部位疼痛	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
胸痛	3 (8.1)	1 (2.7)	5 (12.5)	1 (2.5)	1 (5.3)	0	1 (3.2)	0	10 (7.9)	2 (1.6)
悪寒	4 (10.8)	0	0	0	2 (10.5)	0	0	0	6 (4.7)	0
顔面浮腫	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
顔面痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
疲労	26 (70.3)	3 (8.1)	30 (75.0)	7 (17.5)	13 (68.4)	3 (15.8)	20 (64.5)	1 (3.2)	89 (70.1)	14 (11.0)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)										
全身健康状態低下	2 (5.4)	2 (5.4)	2 (5.0)	2 (5.0)	1 (5.3)	1 (5.3)	0	0	5 (3.9)	5 (3.9)
ヘルニア痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
インフルエンザ様疾患	1 (2.7)	0	2 (5.0)	0	0	0	0	0	3 (2.4)	0
限局性浮腫	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
粘膜の炎症	0	0	2 (5.0)	0	1 (5.3)	1 (5.3)	1 (3.2)	0	4 (3.1)	1 (0.8)
末梢性浮腫	6 (16.2)	0	9 (22.5)	0	2 (10.5)	0	5 (16.1)	0	22 (17.3)	0
発熱	8 (21.6)	0	9 (22.5)	2 (5.0)	6 (31.6)	0	4 (12.9)	0	27 (21.3)	2 (1.6)
肝胆道系障害	1 (2.7)	1 (2.7)	0	0	1 (5.3)	1 (5.3)	1 (3.2)	0	3 (2.4)	2 (1.6)
胆嚢炎	0	0	0	0	1 (5.3)	1 (5.3)	0	0	1 (0.8)	1 (0.8)
肝臓痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
肝静脈血栓症	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
免疫系障害	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
過敏症	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症	11 (29.7)	1 (2.7)	15 (37.5)	5 (12.5)	6 (31.6)	0	11 (35.5)	4 (12.9)	43 (33.9)	10 (7.9)
カテーテル留置部位感染	1 (2.7)	1 (2.7)	1 (2.5)	1 (2.5)	0	0	1 (3.2)	1 (3.2)	3 (2.4)	3 (2.4)
蜂巣炎	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
感染性結膜炎	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
膀胱炎	0	0	3 (7.5)	0	0	0	3 (9.7)	2 (6.5)	6 (4.7)	2 (1.6)
丹毒	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
毛包炎	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
胃腸炎	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
帯状疱疹	0	0	1 (2.5)	0	1 (5.3)	0	0	0	2 (1.6)	0
喉頭炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
リンパ節感染	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
脊髄炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
鼻咽頭炎	1 (2.7)	0	5 (12.5)	0	3 (15.8)	0	3 (9.7)	0	12 (9.4)	0
口腔ヘルペス	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
口腔感染	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
真菌性口腔咽頭炎	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
咽頭炎	2 (5.4)	0	1 (2.5)	1 (2.5)	0	0	2 (6.5)	1 (3.2)	5 (3.9)	2 (1.6)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)										
肺炎	0	0	1 (2.5)	0	0	0	2 (6.5)	2 (6.5)	3 (2.4)	2 (1.6)
鼻炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
敗血症	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
副鼻腔炎	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
皮膚カンジダ	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
皮下組織膿瘍	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
歯感染	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
上気道感染	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
尿路感染	1 (2.7)	0	2 (5.0)	0	0	0	2 (6.5)	0	5 (3.9)	0
傷害、中毒および処置合併症	1 (2.7)	0	2 (5.0)	1 (2.5)	0	0	0	0	3 (2.4)	1 (0.8)
挫傷	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
大腿骨骨折	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
股関節部骨折	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
臨床検査	17 (45.9)	1 (2.7)	15 (37.5)	0	9 (47.4)	1 (5.3)	5 (16.1)	1 (3.2)	46 (36.2)	3 (2.4)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)										
血中アルカリホスファターゼ増加	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
γ－グルタミルトランスフェラーゼ増加	1 (2.7)	1 (2.7)	0	0	1 (5.3)	1 (5.3)	0	0	2 (1.6)	2 (1.6)
体重減少	11 (29.7)	0	12 (30.0)	0	7 (36.8)	0	4 (12.9)	1 (3.2)	34 (26.8)	1 (0.8)
体重増加	5 (13.5)	0	4 (10.0)	0	1 (5.3)	0	1 (3.2)	0	11 (8.7)	0
代謝および栄養障害	11 (29.7)	2 (5.4)	16 (40.0)	1 (2.5)	6 (31.6)	0	11 (35.5)	3 (9.7)	44 (34.6)	6 (4.7)
食欲減退	9 (24.3)	1 (2.7)	15 (37.5)	0	6 (31.6)	0	9 (29.0)	0	39 (30.7)	1 (0.8)
脱水	2 (5.4)	0	0	0	0	0	2 (6.5)	0	4 (3.1)	0
高血糖	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
高マグネシウム血症	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
高トリグリセリド血症	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
低アルブミン血症	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
低カリウム血症	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
低マグネシウム血症	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
肥満	0	0	1 (2.5)	1 (2.5)	0	0	1 (3.2)	1 (3.2)	2 (1.6)	2 (1.6)

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付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害	19 (51.4)	0	17 (42.5)	2 (5.0)	13 (68.4)	0	16 (51.6)	3 (9.7)	65 (51.2)	5 (3.9)
関節痛	6 (16.2)	0	5 (12.5)	0	5 (26.3)	0	3 (9.7)	0	19 (15.0)	0
背部痛	5 (13.5)	0	5 (12.5)	0	4 (21.1)	0	7 (22.6)	1 (3.2)	21 (16.5)	1 (0.8)
単径部痛	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
筋痙縮	1 (2.7)	0	1 (2.5)	0	0	0	1 (3.2)	0	3 (2.4)	0
筋力低下	1 (2.7)	0	1 (2.5)	1 (2.5)	0	0	1 (3.2)	0	3 (2.4)	1 (0.8)
筋骨格系胸痛	1 (2.7)	0	2 (5.0)	0	1 (5.3)	0	0	0	4 (3.1)	0
筋骨格痛	2 (5.4)	0	3 (7.5)	0	0	0	0	0	5 (3.9)	0
筋骨格硬直	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
筋肉痛	7 (18.9)	0	7 (17.5)	0	6 (31.6)	0	6 (19.4)	2 (6.5)	26 (20.5)	2 (1.6)
筋炎	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
四肢痛	2 (5.4)	0	2 (5.0)	1 (2.5)	2 (10.5)	0	5 (16.1)	0	11 (8.7)	1 (0.8)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	10 (27.0)	1 (2.7)	11 (27.5)	0	11 (57.9)	1 (5.3)	19 (61.3)	9 (29.0)	51 (40.2)	11 (8.7)
口唇および口腔内癌	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
悪性胸水	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
腫瘍出血	0	0	0	0	0	0	3 (9.7)	1 (3.2)	3 (2.4)	1 (0.8)

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付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (contd)										
腫瘍疼痛	10 (27.0)	1 (2.7)	11 (27.5)	0	11 (57.9)	1 (5.3)	16 (51.6)	7 (22.6)	48 (37.8)	9 (7.1)
神経系障害	26 (70.3)	3 (8.1)	25 (62.5)	3 (7.5)	8 (42.1)	3 (15.8)	16 (51.6)	4 (12.9)	75 (59.1)	13 (10.2)
前脊髄動脈症候群	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
脳虚血	0	0	1 (2.5)	1 (2.5)	1 (5.3)	1 (5.3)	0	0	2 (1.6)	2 (1.6)
浮動性めまい	6 (16.2)	0	12 (30.0)	0	1 (5.3)	0	8 (25.8)	1 (3.2)	27 (21.3)	1 (0.8)
味覚異常	6 (16.2)	0	7 (17.5)	0	3 (15.8)	0	3 (9.7)	0	19 (15.0)	0
ジスキネジー	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
頭痛	7 (18.9)	0	8 (20.0)	0	1 (5.3)	0	7 (22.6)	0	23 (18.1)	0
記憶障害	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
神経痛	1 (2.7)	0	2 (5.0)	0	0	0	0	0	3 (2.4)	0
起立不耐性	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
嗅覚錯誤	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
末梢性運動ニューロパチー	3 (8.1)	2 (5.4)	3 (7.5)	1 (2.5)	2 (10.5)	1 (5.3)	3 (9.7)	1 (3.2)	11 (8.7)	5 (3.9)
末梢性感覚ニューロパチー	17 (45.9)	2 (5.4)	16 (40.0)	0	7 (36.8)	1 (5.3)	6 (19.4)	1 (3.2)	46 (36.2)	4 (3.1)
傾眠	1 (2.7)	0	1 (2.5)	0	0	0	1 (3.2)	0	3 (2.4)	0

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付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)										
失神	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
精神障害	10 (27.0)	1 (2.7)	12 (30.0)	1 (2.5)	4 (21.1)	0	7 (22.6)	0	33 (26.0)	2 (1.6)
激越	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
不安	2 (5.4)	0	3 (7.5)	0	3 (15.8)	0	4 (12.9)	0	12 (9.4)	0
錯乱状態	1 (2.7)	0	2 (5.0)	1 (2.5)	0	0	1 (3.2)	0	4 (3.1)	1 (0.8)
うつ病	3 (8.1)	0	3 (7.5)	0	1 (5.3)	0	4 (12.9)	0	11 (8.7)	0
不眠症	6 (16.2)	1 (2.7)	5 (12.5)	0	0	0	4 (12.9)	0	15 (11.8)	1 (0.8)
神経症	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
精神病性障害	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
腎および尿路障害	4 (10.8)	1 (2.7)	4 (10.0)	1 (2.5)	0	0	3 (9.7)	1 (3.2)	11 (8.7)	3 (2.4)
膀胱痛	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
排尿困難	1 (2.7)	0	0	0	0	0	1 (3.2)	1 (3.2)	2 (1.6)	1 (0.8)
血尿	0	0	1 (2.5)	0	0	0	1 (3.2)	0	2 (1.6)	0
乏尿	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害 (contd)										
頻尿	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
腎盂腎杯拡張症	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
膿尿	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
腎不全	1 (2.7)	1 (2.7)	1 (2.5)	0	0	0	1 (3.2)	0	3 (2.4)	1 (0.8)
尿管狭窄	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
尿閉	0	0	1 (2.5)	0	0	0	1 (3.2)	0	2 (1.6)	0
生殖系および乳房障害	1 (2.7)	0	4 (10.0)	0	1 (5.3)	0	3 (9.7)	0	9 (7.1)	0
乳房痛	0	0	0	0	0	0	2 (6.5)	0	2 (1.6)	0
不規則月経	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
性器浮腫	0	0	0	0	1 (5.3)	0	1 (3.2)	0	2 (1.6)	0
骨盤不快感	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
膣出血	0	0	3 (7.5)	0	0	0	1 (3.2)	0	4 (3.1)	0
呼吸器、胸郭および縦隔障害	17 (45.9)	1 (2.7)	23 (57.5)	2 (5.0)	13 (68.4)	5 (26.3)	17 (54.8)	3 (9.7)	70 (55.1)	11 (8.7)
慢性閉塞性肺疾患	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)										
咳嗽	6 (16.2)	0	9 (22.5)	0	6 (31.6)	1 (5.3)	9 (29.0)	0	30 (23.6)	1 (0.8)
気管支分泌減少	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
発声障害	1 (2.7)	0	1 (2.5)	0	2 (10.5)	1 (5.3)	0	0	4 (3.1)	1 (0.8)
呼吸困難	10 (27.0)	0	11 (27.5)	2 (5.0)	10 (52.6)	3 (15.8)	10 (32.3)	1 (3.2)	41 (32.3)	6 (4.7)
鼻出血	2 (5.4)	0	1 (2.5)	0	1 (5.3)	0	2 (6.5)	0	6 (4.7)	0
喀血	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
しゃっくり	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
口腔咽頭痛	1 (2.7)	0	2 (5.0)	0	2 (10.5)	0	1 (3.2)	0	6 (4.7)	0
咽頭紅斑	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
胸水	0	0	1 (2.5)	0	1 (5.3)	1 (5.3)	0	0	2 (1.6)	1 (0.8)
胸膜痛	0	0	1 (2.5)	0	0	0	1 (3.2)	0	2 (1.6)	0
肺塞栓症	1 (2.7)	1 (2.7)	0	0	0	0	1 (3.2)	1 (3.2)	2 (1.6)	2 (1.6)
鼻漏	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
喀痰増加	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
上気道閉塞	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
上気道刺激症状	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害	19 (51.4)	0	29 (72.5)	0	10 (52.6)	0	12 (38.7)	0	70 (55.1)	0
ざ瘡	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
脱毛症	16 (43.2)	0	24 (60.0)	0	10 (52.6)	0	11 (35.5)	0	61 (48.0)	0
皮膚乾燥	0	0	2 (5.0)	0	1 (5.3)	0	0	0	3 (2.4)	0
湿疹	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
剥脱性発疹	2 (5.4)	0	6 (15.0)	0	0	0	2 (6.5)	0	10 (7.9)	0
多汗症	2 (5.4)	0	5 (12.5)	0	2 (10.5)	0	1 (3.2)	0	10 (7.9)	0
爪の障害	1 (2.7)	0	1 (2.5)	0	0	0	3 (9.7)	0	5 (3.9)	0
手掌・足底発赤知覚不全症候群	0	0	1 (2.5)	0	1 (5.3)	0	0	0	2 (1.6)	0
そう痒症	2 (5.4)	0	1 (2.5)	0	0	0	2 (6.5)	0	5 (3.9)	0
発疹	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
皮膚亀裂	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
皮膚異常臭	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
皮膚のつっぱり感	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
蕁麻疹	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
外科および内科処置	1 (2.7)	1 (2.7)	1 (2.5)	0	0	0	0	0	2 (1.6)	1 (0.8)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-4
Study 207
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
外科および内科処置 (contd)										
回腸手術	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
悪性腫瘍摘除	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
血管障害	7 (18.9)	2 (5.4)	7 (17.5)	0	5 (26.3)	1 (5.3)	5 (16.1)	0	24 (18.9)	3 (2.4)
深部静脈血栓症	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
塞栓症	1 (2.7)	0	1 (2.5)	0	1 (5.3)	0	0	0	3 (2.4)	0
潮紅	0	0	3 (7.5)	0	0	0	0	0	3 (2.4)	0
血腫	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
高血圧	3 (8.1)	0	2 (5.0)	0	1 (5.3)	0	1 (3.2)	0	7 (5.5)	0
低血圧	0	0	1 (2.5)	0	2 (10.5)	0	2 (6.5)	0	5 (3.9)	0
リンパ浮腫	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
蒼白	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
骨盤静脈血栓症	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
静脈炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
大静脈塞栓症	0	0	0	0	1 (5.3)	1 (5.3)	0	0	1 (0.8)	1 (0.8)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_4.sas 18JUN201513:42

付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any treatment-related TEAEs	35 (94.6)	13 (35.1)	35 (87.5)	7 (17.5)	18 (94.7)	9 (47.4)	26 (83.9)	4 (12.9)	114 (89.8)	33 (26.0)
血液およびリンパ系障害	3 (8.1)	3 (8.1)	2 (5.0)	2 (5.0)	3 (15.8)	3 (15.8)	2 (6.5)	1 (3.2)	10 (7.9)	9 (7.1)
発熱性好中球減少症	3 (8.1)	3 (8.1)	1 (2.5)	1 (2.5)	2 (10.5)	2 (10.5)	1 (3.2)	1 (3.2)	7 (5.5)	7 (5.5)
リンパ節痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
好中球減少症	0	0	1 (2.5)	1 (2.5)	1 (5.3)	1 (5.3)	0	0	2 (1.6)	2 (1.6)
心臓障害	1 (2.7)	0	1 (2.5)	0	0	0	1 (3.2)	0	3 (2.4)	0
狭心症	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
第一度房室ブロック	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
動悸	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
耳および迷路障害	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
耳痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
眼障害	3 (8.1)	0	2 (5.0)	0	0	0	0	0	5 (3.9)	0
眼乾燥	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_5.sas 19JUN201513:24

付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
眼障害 (contd)										
流涙増加	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
オキュラーサーフェス疾患	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
霧視	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
胃腸障害	27 (73.0)	3 (8.1)	25 (62.5)	0	15 (78.9)	1 (5.3)	16 (51.6)	1 (3.2)	83 (65.4)	5 (3.9)
腹部膨満	3 (8.1)	0	1 (2.5)	0	0	0	0	0	4 (3.1)	0
腹痛	2 (5.4)	0	1 (2.5)	0	1 (5.3)	0	3 (9.7)	0	7 (5.5)	0
上腹部痛	0	0	0	0	1 (5.3)	0	1 (3.2)	0	2 (1.6)	0
肛門出血	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
便秘	3 (8.1)	0	8 (20.0)	0	2 (10.5)	0	3 (9.7)	0	16 (12.6)	0
下痢	7 (18.9)	0	7 (17.5)	0	4 (21.1)	1 (5.3)	5 (16.1)	0	23 (18.1)	1 (0.8)
口内乾燥	0	0	1 (2.5)	0	0	0	3 (9.7)	0	4 (3.1)	0
消化不良	1 (2.7)	0	1 (2.5)	0	0	0	2 (6.5)	0	4 (3.1)	0
鼓腸	1 (2.7)	0	1 (2.5)	0	0	0	2 (6.5)	0	4 (3.1)	0
排便回数増加	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
消化器痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_5.sas 19JUN201513:24

付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)										
胃食道炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
歯肉炎	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
悪心	15 (40.5)	1 (2.7)	11 (27.5)	0	9 (47.4)	0	8 (25.8)	0	43 (33.9)	1 (0.8)
食道痛	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
口腔内痛	0	0	0	0	1 (5.3)	0	2 (6.5)	0	3 (2.4)	0
歯周病	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
口内炎	5 (13.5)	2 (5.4)	9 (22.5)	0	3 (15.8)	0	7 (22.6)	1 (3.2)	24 (18.9)	3 (2.4)
上部消化管出血	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
嘔吐	8 (21.6)	1 (2.7)	4 (10.0)	0	3 (15.8)	0	5 (16.1)	0	20 (15.7)	1 (0.8)
一般・全身障害および投与部位の状態	25 (67.6)	3 (8.1)	26 (65.0)	3 (7.5)	13 (68.4)	3 (15.8)	17 (54.8)	0	81 (63.8)	9 (7.1)
カテーテル留置部位疼痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
胸痛	1 (2.7)	0	2 (5.0)	0	0	0	1 (3.2)	0	4 (3.1)	0
悪寒	4 (10.8)	0	0	0	2 (10.5)	0	0	0	6 (4.7)	0
疲労	23 (62.2)	3 (8.1)	21 (52.5)	3 (7.5)	10 (52.6)	2 (10.5)	16 (51.6)	0	70 (55.1)	8 (6.3)
全身健康状態低下	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_5.sas 19JUN201513:24

付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)										
インフルエンザ様疾患	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
限局性浮腫	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
粘膜の炎症	0	0	1 (2.5)	0	1 (5.3)	1 (5.3)	1 (3.2)	0	3 (2.4)	1 (0.8)
末梢性浮腫	2 (5.4)	0	4 (10.0)	0	0	0	0	0	6 (4.7)	0
発熱	6 (16.2)	0	6 (15.0)	0	1 (5.3)	0	3 (9.7)	0	16 (12.6)	0
肝胆道系障害	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
肝臓痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
免疫系障害	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
過敏症	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
感染症および寄生虫症	4 (10.8)	0	3 (7.5)	1 (2.5)	2 (10.5)	0	4 (12.9)	2 (6.5)	13 (10.2)	3 (2.4)
蜂巣炎	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
膀胱炎	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
丹毒	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_6_5.sas 19JUN201513:24

付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)										
帯状疱疹	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
腎盂炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
鼻咽頭炎	1 (2.7)	0	1 (2.5)	0	1 (5.3)	0	0	0	3 (2.4)	0
口腔ヘルペス	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
咽頭炎	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
肺炎	0	0	0	0	0	0	2 (6.5)	2 (6.5)	2 (1.6)	2 (1.6)
尿路感染	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
臨床検査	9 (24.3)	1 (2.7)	6 (15.0)	0	3 (15.8)	1 (5.3)	3 (9.7)	0	21 (16.5)	2 (1.6)
血中アルカリホスファターゼ増加	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
γ－グルタミルトランスフェラーゼ増加	1 (2.7)	1 (2.7)	0	0	1 (5.3)	1 (5.3)	0	0	2 (1.6)	2 (1.6)
体重減少	7 (18.9)	0	6 (15.0)	0	2 (10.5)	0	2 (6.5)	0	17 (13.4)	0
体重増加	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
代謝および栄養障害	8 (21.6)	1 (2.7)	10 (25.0)	0	4 (21.1)	0	9 (29.0)	1 (3.2)	31 (24.4)	2 (1.6)
食欲減退	6 (16.2)	0	10 (25.0)	0	4 (21.1)	0	8 (25.8)	0	28 (22.0)	0

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付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
代謝および栄養障害 (contd)										
高トリグリセリド血症	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
低アルブミン血症	1 (2.7)	1 (2.7)	0	0	0	0	0	0	1 (0.8)	1 (0.8)
低カリウム血症	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
筋骨格系および結合組織障害	8 (21.6)	0	6 (15.0)	0	5 (26.3)	0	7 (22.6)	1 (3.2)	26 (20.5)	1 (0.8)
関節痛	2 (5.4)	0	1 (2.5)	0	2 (10.5)	0	2 (6.5)	0	7 (5.5)	0
背部痛	3 (8.1)	0	0	0	1 (5.3)	0	1 (3.2)	0	5 (3.9)	0
筋痙縮	1 (2.7)	0	1 (2.5)	0	0	0	1 (3.2)	0	3 (2.4)	0
筋力低下	1 (2.7)	0	0	0	0	0	1 (3.2)	0	2 (1.6)	0
筋骨格痛	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
筋骨格硬直	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
筋肉痛	4 (10.8)	0	3 (7.5)	0	2 (10.5)	0	3 (9.7)	1 (3.2)	12 (9.4)	1 (0.8)
筋炎	0	0	0	0	0	0	1 (3.2)	1 (3.2)	1 (0.8)	1 (0.8)
四肢痛	0	0	0	0	1 (5.3)	0	2 (6.5)	0	3 (2.4)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	0	0	1 (5.3)	0	4 (12.9)	0	5 (3.9)	0

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付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (contd)										
腫瘍疼痛	0	0	0	0	1 (5.3)	0	4 (12.9)	0	5 (3.9)	0
神経系障害	23 (62.2)	3 (8.1)	22 (55.0)	2 (5.0)	7 (36.8)	2 (10.5)	9 (29.0)	1 (3.2)	61 (48.0)	8 (6.3)
脳虚血	0	0	1 (2.5)	1 (2.5)	0	0	0	0	1 (0.8)	1 (0.8)
浮動性めまい	3 (8.1)	0	9 (22.5)	0	1 (5.3)	0	5 (16.1)	0	18 (14.2)	0
味覚異常	6 (16.2)	0	6 (15.0)	0	2 (10.5)	0	2 (6.5)	0	16 (12.6)	0
頭痛	5 (13.5)	0	5 (12.5)	0	0	0	4 (12.9)	0	14 (11.0)	0
神経痛	1 (2.7)	0	2 (5.0)	0	0	0	0	0	3 (2.4)	0
起立不耐性	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
末梢性運動ニューロパチー	3 (8.1)	2 (5.4)	3 (7.5)	1 (2.5)	2 (10.5)	1 (5.3)	1 (3.2)	0	9 (7.1)	4 (3.1)
末梢性感覚ニューロパチー	17 (45.9)	2 (5.4)	15 (37.5)	0	7 (36.8)	1 (5.3)	5 (16.1)	1 (3.2)	44 (34.6)	4 (3.1)
精神障害	1 (2.7)	0	3 (7.5)	0	0	0	0	0	4 (3.1)	0
不眠症	1 (2.7)	0	2 (5.0)	0	0	0	0	0	3 (2.4)	0
神経症	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0

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付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害	0	0	2 (5.0)	0	0	0	2 (6.5)	0	4 (3.1)	0
乏尿	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
頻尿	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
膿尿	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
腎不全	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
生殖系および乳房障害	0	0	1 (2.5)	0	0	0	1 (3.2)	0	2 (1.6)	0
乳房痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
膣出血	0	0	1 (2.5)	0	0	0	1 (3.2)	0	2 (1.6)	0
呼吸器、胸郭および縦隔障害	6 (16.2)	0	8 (20.0)	1 (2.5)	6 (31.6)	2 (10.5)	7 (22.6)	0	27 (21.3)	3 (2.4)
咳嗽	2 (5.4)	0	2 (5.0)	0	2 (10.5)	1 (5.3)	3 (9.7)	0	9 (7.1)	1 (0.8)
発声障害	1 (2.7)	0	0	0	1 (5.3)	1 (5.3)	0	0	2 (1.6)	1 (0.8)
呼吸困難	3 (8.1)	0	4 (10.0)	1 (2.5)	3 (15.8)	1 (5.3)	4 (12.9)	0	14 (11.0)	2 (1.6)
鼻出血	1 (2.7)	0	0	0	1 (5.3)	0	1 (3.2)	0	3 (2.4)	0
しゃっくり	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
口腔咽頭痛	0	0	0	0	2 (10.5)	0	0	0	2 (1.6)	0

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付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)										
咽頭紅斑	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
胸膜痛	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
上気道閉塞	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
上気道刺激症状	0	0	1 (2.5)	0	0	0	0	0	1 (0.8)	0
皮膚および皮下組織障害	18 (48.6)	0	27 (67.5)	0	9 (47.4)	0	12 (38.7)	0	66 (52.0)	0
ざ瘡	0	0	0	0	1 (5.3)	0	0	0	1 (0.8)	0
脱毛症	15 (40.5)	0	22 (55.0)	0	9 (47.4)	0	11 (35.5)	0	57 (44.9)	0
皮膚乾燥	0	0	2 (5.0)	0	1 (5.3)	0	0	0	3 (2.4)	0
剥脱性発疹	2 (5.4)	0	6 (15.0)	0	0	0	2 (6.5)	0	10 (7.9)	0
多汗症	1 (2.7)	0	4 (10.0)	0	0	0	0	0	5 (3.9)	0
爪の障害	1 (2.7)	0	1 (2.5)	0	0	0	3 (9.7)	0	5 (3.9)	0
手掌・足底発赤知覚不全症候群	0	0	1 (2.5)	0	1 (5.3)	0	0	0	2 (1.6)	0
そう痒症	1 (2.7)	0	1 (2.5)	0	0	0	2 (6.5)	0	4 (3.1)	0
発疹	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
皮膚亀裂	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0

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付録 2.7.6-5
Study 207
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

MedDRA System Organ Class Preferred Term	ADI (N=37)		LMS (N=40)		SYN (N=19)		Other (N=31)		Total (N=127)	
	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)										
皮膚のつっぱり感	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
蕁麻疹	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0
血管障害	2 (5.4)	0	1 (2.5)	0	1 (5.3)	0	2 (6.5)	0	6 (4.7)	0
高血圧	1 (2.7)	0	1 (2.5)	0	0	0	0	0	2 (1.6)	0
低血圧	0	0	0	0	1 (5.3)	0	1 (3.2)	0	2 (1.6)	0
蒼白	0	0	0	0	0	0	1 (3.2)	0	1 (0.8)	0
静脈炎	1 (2.7)	0	0	0	0	0	0	0	1 (0.8)	0

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付録 2.7.6-6　死亡又は重篤な有害事象の被験者ごとの叙述（外国 207 試験）

死亡又は死亡以外の重篤な有害事象が認められた被験者に関する叙述を以下に示した。

被験者番号	転帰が死亡の重篤な有害事象	死亡以外の重篤な有害事象
0101-0094		x
0101-0125		x
0147-0001		x
0147-0004		x
0147-0012		x
0147-0019	x	x
0147-0025		x
0147-0034		x
0147-0037		x
0147-0065		x
0147-0095		x
0225-0069		x
0225-0075		x
0225-0076		x
0225-0111		x
0227-0082		x
0227-0090		x
0227-0091		x
0227-0108		x
0227-0127	x	
0228-0057		x
0228-0087		x
0228-0119		x
0287-0098		x
0287-0128		x
0406-0002		x
0406-0005		x
0406-0013		x
0406-0020		x
0440-0072		x
0440-0096		x
0509-0009		x
0509-0051		x
0509-0123		x
0509-0126		x
0527-0039		x
0527-0046		x
0527-0088		x
0527-0120		x
0528-0036		x
0528-0042		x
0528-0074	x	
0530-0016		x
0530-0018		x
0550-0031		x
0550-0115		x
3039-0029		x

転帰が死亡の重篤な有害事象（3 例）

被験者番号	0147-0019
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 7 サイクル（134 日間）
投与期間	[redacted]年[redacted]月[redacted]日～[redacted]年[redacted]月[redacted]日
叙述の理由	
転帰が死亡の重篤な有害事象	全身健康状態低下/General deterioration
死亡以外の重篤な有害事象	関節痛/Arthralgia, 腟出血/Vaginal bleeding, 全身健康状態低下/General deterioration, 大腿骨骨折/Femoral fracture

Subject 0147-0019, a 72-year-old female was initially diagnosed with Stage 3 leiomyosarcoma on 13 October 2004. At screening on Day -1 * , tumor assessment via CT scan included lung metastases, abdominal wall metastasis, paraaortal mass, and pelvis metastasis. Prior medical and surgical history included anxiety, arterial hypertension, right eye corneal erosion, hypercholesterolemia, insomnia, right hip coxarthrosis, nephrectomy, and depression. Prior chemotherapies included doxorubicin and ifosfamide. Previous radiotherapy was not reported. Prior medications taken and discontinued within 30 days of first dose of study drug included naproxen.

On Day 1 * , the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included acetaminophen, acetylsalicylic acid, alizapride, alprazolam, amitriptyline, atorvastatin, bisoprolol, doxepin, fentanyl, furosemide, haloperidol, ibuprofen, lactulose, levofloxacin, metoclopramide, midazolam, morphine, mucositis cocktail, olmesartan, omeprazole, oxycodone, paroxetine, potassium, propofol, naproxen, spironolactone, tramadol, and zolpidem.

On [redacted] (Day 72), the subject developed vaginal bleeding (CTCAE Grade 1). There was no drug treatment for the vaginal bleeding. The study drug dose was delayed and reduced to 1.1 mg/m^2 as a result of the vaginal bleeding. The event of vaginal bleeding resolved on [redacted] (Day 73). This event lasted 2 days and was reported by the investigator as not related to the study drug.

On [redacted] (Day 134) the subject received her last dose of study drug and was discontinued from treatment due to nonserious adverse events. The subject had received 7 cycles of study drug.

On [redacted] (Day 145), the subject experienced general deterioration (CTCAE Grade 4) and femoral column fracture (CTCAE Grade 2). There was no drug treatment for the general deterioration or femoral column fracture. On [redacted] (Day 152) the subject's general deterioration worsened to CTCAE Grade 5 and the subject died. The events of general deterioration, femoral column fracture, and general deterioration leading to death were reported by the investigator as not related to the study drug. Other relevant events occurring during treatment were not reported.

* 新薬承認情報提供時に置き換え

被験者番号	0227-0127
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 1 サイクル（9 日間）
投与期間	[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 年 [redacted] 月 [redacted] 日
叙述の理由	
転帰が死亡の重篤な有害事象	悪性胸水/Malignant pleural effusion

Subject 0227-0127, a 52-year-old male, was initially diagnosed with Stage 2 retroperitoneal liposarcoma 14 May 2008. At screening on Day −8 *, tumor assessment via CT scan included mediastinal lesion and pleural effusion. Prior medical and surgical history included asthenia. Prior chemotherapies included doxorubicin. Previous radiotherapy was not reported. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included acetaminophen, amiodarone, bromazepam, bumetanide, clonazepam, digoxin, diltiazepam, furosemide, gabapentin, hydroxyzine, lactulose, Lansoyl (mineral oil), morphine, oxycodone, polyethylene glycol, and tetrazepam.

On [redacted] (Day 9) the subject received the last dose of study drug. The subject had received 1 cycle of study drug.

On [redacted] (Day 12) the subject died from pleural effusion (CTCAE Grade 5). Prior to death the subject was treated with acetaminophen, Dafalgan (acetaminophen/codeine), and furosemide. At study entry the subject was experiencing a Grade 2 pleural effusion which was considered serious. This event lasted until the subject's death. The bilateral pleural effusion was reported by the investigator as not related to the study drug. Other relevant events occurring during treatment were not reported.

* 新薬承認情報提供時に置き換え

被験者番号	0528-0074
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 3 サイクル（57 日間）
投与期間	[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 年 [redacted] 月 [redacted] 日
叙述の理由	
転帰が死亡の重篤な有害事象	脳虚血/Cerebrovascular ischemia

Subject 0528-0074, a 76-year-old female was initially diagnosed with Stage 3 leiomyosarcoma on 05 April 2007. At screening, tumor assessment via CT scan included multiple liver metastases and lung metastasis. Prior medical and surgical history included hypothyroidism, thyroidectomy, percutaneous transluminal angioplasty, arterial hypertension, inferior myocardial infarction, hypercholesterolemia, coronary bypass, congestive heart failure, clopidogrel resistance, and curative surgery. Prior chemotherapies included doxorubicin. Previous radiotherapy was not reported. Prior medications taken and discontinued within 30 days of first dose of study drug included phenprocoumon.

On Day 1 * the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included acetylsalicylic acid, bisoprolol, dalteparin, enoxaparin, hydrochlorothiazide, levothyroxine, omeprazole, ramipril, simvastatin, and torasemide.

On [redacted] (Day 57) the subject received the last dose of study drug. On [redacted] (Day 64) the subject withdrew from study due to adverse event. The subject had received 3 cycles of study drug.

From [redacted] (Day 66) to [redacted] (Day 94) the subject suffered from cerebrovascular ischemia resulting in her death (CTCAE Grade 5). The subject was treated with enoxaparin for apoplexy resulting from the cerebrovascular ischemia. The cerebrovascular ischemia lasted 29 days and was reported by the investigator to be possibly related to treatment.

Other relevant events occurring during treatment were not reported.

In the sponsor's opinion, the relationship of the study drug to the event of cerebrovascular ischemia resulting in death is unclear with the data available. However, in consideration of the subject's clinical history upon study entry, the relationship is unlikely.

* 新薬承認情報提供時に置き換え

死亡以外のその他の重篤な有害事象（44 例）

被験者番号	0101-0094
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 4 サイクル（71 日間）
投与期間	[redacted]年[redacted]月[redacted]日～[redacted]年[redacted]月[redacted]日
叙述の理由	
死亡以外の重篤な有害事象	末梢性運動ニューロパチー/Motor neuropathy，末梢性感覚ニューロパチー/Sensory neuropathy

Subject 0101-0094, a 59-year-old female, was initially diagnosed with Grade 3 retroperitoneal adipocytic liposarcoma on 02 August 2005. At screening on Day −3 *, tumor assessment via CT scan included left hypochondria mass and left iliac crest mass. Prior medical and surgical history included hypertension, hypercholesterolemia, diabetes type 2, and curative surgery. Prior chemotherapies included doxorubicin and ifosfamide. Previous radiotherapy was not reported. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included bisoprolol, domperidone, filgrastim, gliclazide, insulin, metformin, mouthwash (salicylate of soda) repaglinide, rosiglitazone, rosuvastatin, and tramadol.

On [redacted] (Day 71) the subject received her last dose of study drug and was discontinued from treatment due to nonserious adverse events. The subject received 4 cycles of study drug.

On [redacted] (Day 85) the subject experienced both motor neuropathy (CTCAE Grade 3) and sensory neuropathy (CTCAE Grade 1). No treatment was recorded for the neuropathies. This event was ongoing at the end of the 30-day follow up period. The motor neuropathy was reported by the investigator as probably related to the study drug, and the sensory neuropathy was reported by the investigator as possibly related to the study drug. Other relevant events occurring during treatment were not reported.

* 新薬承認情報提供時に置き換え

被験者番号	0101-0125
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 12 サイクル（241 日間）
投与期間	[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 年 [redacted] 月 [redacted] 日
叙述の理由	
死亡以外の重篤な有害事象	嘔吐/Vomiting，腸閉塞/Gastric obstruction，腹部癒着/Abdominal adhesions

Subject 0101-0125, a 60-year-old male, was initially diagnosed with Grade 2 retroperitoneal liposarcoma on 20 January 2003. At screening on Day −4 *, tumor assessment via CT scan included aorta primary tumor lesion, right flank lymph node lesion, right psoas lymph node lesion, right kidney mass, central retroperitoneal mass, hepatic angioma, and superior and mediastinal lymph nodes adenopathy. Prior medical and surgical history included anxiety, hypertension, asthma, diabetes mellitus, and palliative surgery. Prior chemotherapies were not reported. Previous radiotherapy excluded hematopoietic sites. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing and concomitant medications received during treatment included acetylsalicylic acid, bisoprolol, metoclopramide, Mixtard 30 (insulin/biphasic isophane), molsidomine, rabeprazole, and tiotropium.

On [redacted] (Day 14) the subject experienced vomiting (CTCAE Grade 3). The subject was treated with metoclopramide. The study drug was not changed. This event resolved on [redacted] (Day 17). The vomiting lasted 4 days and was reported by the investigator as not related to the study drug.

On [redacted] (Day 92) the subject developed gastric obstruction (CTCAE Grade 3). The administration of the study medication was delayed. This event resolved on [redacted] (Day 98). The obstruction lasted 7 days and was reported by the investigator as not related to the study drug. Other relevant events occurring during treatment included nausea.

On [redacted] (Day 241) the subject received his last dose of study drug and was discontinued due to lack of therapeutic efficacy. The subject had received 12 cycles of study drug.

* 新薬承認情報提供時に置き換え

被験者番号	0147-0001
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 23 サイクル（377 日間）
投与期間	[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 年 [redacted] 月 [redacted] 日
叙述の理由	
死亡以外の重篤な有害事象	肺塞栓症/Pulmonary embolism

Subject 0147-0001, a 25-year-old female, was initially diagnosed with Grade 2 fibroblastic tumor on 04 February 2002. At screening on Day −21 *, tumor assessment via CT scan included multiple bilateral lung lesions, right spinal cord lesion, and right lymph node lesion. Prior medical and surgical history included pneumonia, appendectomy, allergy to contrast, deep venous thrombosis, and curative surgery. Prior chemotherapies included doxorubicin. Previous radiotherapy included radiation to the hematopoietic sites. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing and concomitant medications received during treatment included acetaminophen, alizapride, amoxicillin, amitriptyline, cetirizine, darbepoetin alfa, diclofenac, fentanyl, ferricure drops (iron hydroxide poly maltose complex), hydromorphone, iron, levofloxacin, magnesium oxide, morphine, moxifloxacin, Mercilon (ethinylestradiol/desogestrel), methylprednisolone, Mycolog cream (nystatin/triamcinolone), norfloxacin, omeprazole, pregabalin, sodium citrate, sodium picosulfate, tinzaparin, tramadol, and venlafaxine.

On [redacted] (Day 57), the subject experienced a pulmonary embolism (CTCAE Grade 4). The subject was hospitalized and treated with nadroparin. The study drug dose was not changed as a result of the pulmonary embolism. This event resolved on [redacted] (Day 61). The pulmonary embolism lasted 5 days and was reported by the investigator as not related to treatment.

On [redacted] (Day 377) the subject received her last dose of study drug and was discontinued from treatment due to lack of therapeutic efficacy. The subject had received 23 cycles of study drug.

* 新薬承認情報提供時に置き換え

被験者番号	0147-0004
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 10 サイクル（191 日間）
投与期間	[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 年 [redacted] 月 [redacted] 日
叙述の理由	
死亡以外の重篤な有害事象	肺炎/Pneumonia

Subject 0147-0004, a 55-year-old male, was initially diagnosed with Grade 3 moderately differentiated soft tissue sarcoma on 10 July 2000. At screening on Day −23 *, tumor assessment via CT scan included multiple liver lesions. Prior medical and surgical history included insomnia, polyneuropathy, mycosis, and palliative surgery. Prior chemotherapies included doxorubicin and ifosfamide. Previous radiotherapy excluded hematopoietic sites. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included acetaminophen, amitriptyline, amoxicillin clavulanate, etilefrine, gabapentin, nifedipine, terbinafine, tramadol, and zolpidem.

On [redacted] (Day 152) the subject developed pneumonia (CTCAE Grade 3). The subject was hospitalized and treated with IV amoxicillin clavulanate. Latest blood tests during the admission showed neutropenia (neutrophils = 4.8 × 10^9/L) and leucopenia (WBC = 5.8 × 10^9/L). The study drug dose was not changed as a result of pneumonia. This event resolved on [redacted] (Day 157). The pneumonia lasted 6 days and was reported by the investigator to be possibly related to the study drug. Other relevant events occurring during treatment included leukopenia, neutropenia, and stomatitis.

On [redacted] (Day 191) the subject received his last dose of study drug and was discontinued from treatment due to lack of therapeutic efficacy. The subject received 10 cycles of study drug.

* 新薬承認情報提供時に置き換え

被験者番号	0147-0012
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 14 サイクル（288 日間）
投与期間	[redacted]年[redacted]月[redacted]日～[redacted]年[redacted]月[redacted]日
叙述の理由	
死亡以外の重篤な有害事象	四肢痛/Pain in extremity，失神/Syncope

Subject 0147-0012, a 27-year-old female, was initially diagnosed with Grade 2 lower extremity smooth muscle leiomyosarcoma on 29 December 2006. At screening on Day -6 * , tumor assessment via CT scan included lesions in the lungs, inguinal lymph nodes, and primary tumor of the right lower leg; via clinical exam included lesions of the skin of right lower leg. Prior medical and surgical history included depression and biopsy of the calf. Prior chemotherapies included doxorubicin and ifosfamide. Previous radiotherapy was not reported. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 * , the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included acetaminophen, azithromycin, Diane (cyproterone/ethinyl estradiol), doxycycline, flucloxacillin, lymecycline, Microgynon (ethinylestradiol/levonorgestrel), omeprazole, paroxetine, and tramadol.

On [redacted] (Day 288) the subject experienced musculoskeletal pain in the left arm (CTCAE Grade 3) and syncope (CTCAE Grade 3). The subject was hospitalized and treated with methylprednisolone and valproic acid for syncope. The study drug dose was discontinued as a result of syncope. The syncope resolved on [redacted] (Day 289), lasted 2 days, and was reported by the investigator to be not related to the study drug. The musculoskeletal pain in the left arm was ongoing at the end of the 30-day follow up period and was reported to be not related to the study drug. Other relevant events occurring during treatment were not reported.

The subject received her last dose of study drug on [redacted] (Day 288) and was discontinued from treatment due to lack of therapeutic efficacy. The subject had received 14 cycles of study drug.

* 新薬承認情報提供時に置き換え

被験者番号	0147-0025
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 2 サイクル（29 日間）
投与期間	[redacted] 年 [redacted] 月 [redacted] 日～[redacted] 年 [redacted] 月 [redacted] 日
叙述の理由	
死亡以外の重篤な有害事象	貧血/Anemia，低カリウム血症/Hypokalemia

Subject 0147-0025, a 60-year-old male, was initially diagnosed with Grade 2 epithelioid sarcoma on 12 December 2005. At screening on Day −9 *, tumor assessment via CT scan included left perineal region metastasis and right lymph node metastasis. Prior medical and surgical history included anemia, hypertension, depression, insomnia, prostatism symptom, hypokalemia, and palliative surgery. Prior chemotherapies included doxorubicin. Previous radiotherapy was not reported. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included escitalopram, furosemide, lactulose, mirtazapine, potassium chloride, packed red blood cells, potassium gluconate, tamsulosin, tramadol, and zolpidem.

On [redacted] (Day 29) the subject received his last dose of study drug and was discontinued from treatment due to lack of therapeutic efficacy. The subject had received 2 cycles of study drug.

On [redacted] (Day 36) the subject was diagnosed with anemia (CTCAE Grade 4) and hypokalemia (CTCAE Grade 3). The subject was hospitalized due to hypokalemia. Laboratory results showed RBC = 1.87×10^9/L (baseline = 2.79×10^9/L) and potassium = 2.6 mmol/L (baseline = 3.4 mmol/L). He was treated with packed cells, furosemide, and potassium chloride. The event of hypokalemia resolved on [redacted] (Day 40), lasted 5 days, and was reported by the investigator as possibly related to the study drug. The event of anemia was ongoing at the time of subject's death on Day 125 * and was reported by the investigator to be not related to treatment. Other relevant events were not reported.

In the sponsor's opinion, the event of hypokalemia is possibly related to study drug.

* 新薬承認情報提供時に置き換え

被験者番号	0147-0034
投与量/投与方法	21 日間を 1 サイクルとし，各サイクル第 1 日目及び第 8 日目に本薬 1.4 mg/m^2 を投与
最終投与時のサイクル（投与期間）	第 3 サイクル（51 日間）
投与期間	[redacted]年[redacted]月[redacted]日～[redacted]年[redacted]月[redacted]日
叙述の理由	
死亡以外の重篤な有害事象	発熱性好中球減少症/Febrile neutropenia

Subject 0147-0034, a 67-year-old male, was initially diagnosed with Grade 2 adipocytic sarcoma (liposarcoma) on 20 August 2003. At screening on Day −2 *, tumor assessment via CT scan included pleural effusion, multiple left lung metastases, and liver metastasis. Prior medical and surgical history included cardiac stenosis of the second lateral branch, hyperlipidemia, myocardial hypertrophy, hepatic steatosis, gout, cholecystolithiasis, diabetes, and curative surgery. Prior chemotherapies included doxorubicin. Previous radiotherapy excluded hematopoietic sites. Prior medications taken and discontinued within 30 days of first dose of study drug were not reported.

On Day 1 *, the subject started treatment. Prior medications ongoing during treatment and concomitant medications received during treatment included acetaminophen, acetylsalicylic acid, allopurinol, atenolol, ceftazidime, clindamycin, fenofibrate, metformin, packed red blood cells, pravastatin, and tramadol.

On [redacted] (Day 12) the subject was diagnosed with febrile neutropenia (CTCAE Grade 3). The neutrophils were 0.1 × 10^9/L, and WBC 0.5 × 10^9/L. The subject was hospitalized and treated with ceftazidime and clindamycin. The study drug dose was reduced to 1.1 mg/m^2. This event resolved on [redacted] (Day 20). The febrile neutropenia lasted 9 days and was reported by the investigator as probably related to the study drug. Other relevant events occurring during treatment were not reported.

On [redacted] (Day 51) the subject received his last dose of study medication and was discontinued from treatment due to lack of therapeutic efficacy. The subject had received 3 cycles of study drug.

* 新薬承認情報提供時に置き換え