2 STUDY SYNOPSIS

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<th>Name of Company:</th>
<th>Eisai Co., Ltd.</th>
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<tr>
<td>Name of Finished Product:</td>
<td>Halaven®, injection for intravenous administration</td>
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<tr>
<td>Name of Active Ingredient:</td>
<td>Eribulin mesilate (JAN)</td>
</tr>
<tr>
<td>INDIVIDUAL STUDY TABLE</td>
<td>Referring to Module 5 of the Dossier</td>
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<td>(For National Authority Use Only)</td>
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Study Title
An Open-label, Multi-center, Phase 2 Study to Evaluate the Efficacy and Safety of Eribulin in Previously Treated Subjects with Advanced or Metastatic Soft Tissue Sarcoma

Investigator(s)/Site(s)
Kazuo Isu, MD (coordinating investigator), et al.
Multicenter: 13 sites in Japan (refer to Appendix 16.1.4.1 for the list of investigators and sites)

Publication (Reference)
None

Study Period
14 Nov 2011 (first subject’s signed informed consent) to 14 Nov 2014 (data cutoff)

Phase of Development
Phase 2

Objectives
Primary objectives:
- To evaluate the efficacy of eribulin mesilate, as measured by progression-free rate at 12 weeks (PFR12wks), in subjects with advanced or metastatic soft tissue sarcoma (STS), 1 of 2 subtypes: adipocytic sarcoma (ADI) or leiomyosarcoma (LMS) previously treated with chemotherapy.
- To evaluate the efficacy of eribulin mesilate, as measured by PFR12wks in subjects with advanced or metastatic STSs other than ADI/LMS (other types of eligible soft tissue sarcoma [OTH]) previously treated with chemotherapy.

Secondary objectives:
- To evaluate the efficacy of eribulin mesilate, as measured by the following, in subjects with advanced or metastatic STS, 1 of 2 subtypes: ADI or LMS previously treated with chemotherapy.
  - Progression-free survival (PFS)
  - Overall survival (OS)
  - Objective response rate (ORR = the proportion of complete response [CR] + partial response [PR])
  - Disease control rate (DCR = the proportion of CR + PR + stable disease [SD])
  - Clinical benefit rate (CBR = the proportion of CR + PR + durable stable disease [dSD], duration of SD ≥11 weeks)
  - Durable stable disease rate (dSDR = the proportion of dSD)
- To evaluate the efficacy of eribulin mesilate, as measured by PFS, OS, ORR, DCR, CBR, and dSDR, in
subjects with advanced or metastatic STSs of OTH previously treated with chemotherapy.

- To evaluate the safety of eribulin mesilate in subjects with advanced or metastatic STS (including all subtypes) previously treated with chemotherapy.

- To explore the efficacy of eribulin mesilate, as measured by PFR_{12wks}, PFS, OS, ORR, DCR, CBR, and dSDR, in subjects with advanced or metastatic STS (including all subtypes) previously treated with chemotherapy.

- To investigate pharmacokinetics of eribulin mesilate, in subjects with advanced or metastatic STS (including all subtypes) previously treated with chemotherapy.

Methodology
This was a Phase 2, multi-center, open-label, nonrandomized study to evaluate the efficacy and safety of eribulin mesilate in subjects with advanced or metastatic STS who had been previously treated with chemotherapy.

The study consisted of a Pre-treatment Period, a Treatment Period, and a Posttreatment Period. The Pretreatment Period included obtaining informed consent, screening assessment, and baseline assessment, which was performed within 28 days and 7 days before the start of study treatment, respectively.

The Treatment Period started with the first administration of study drug on Day 1 of Cycle 1, and treatment continued until progressive disease (PD) was confirmed according to RECIST (Response Evaluation Criteria in Solid Tumors) version 1.1, or any of the criteria for discontinuation of study treatment for individual subjects became applicable (see Duration of Treatment). During the Treatment Period, the subjects underwent regular assessments for safety and tumor response. The objective evaluation of tumor response was performed according to RECIST 1.1 every 6 weeks until PD was confirmed.

The Posttreatment Period included post treatment visits (last observation) and a follow-up examination. The post treatment assessment was performed 30 days (±3 days) after the last dose of study drug. Subjects who discontinued study treatment before PD was confirmed based on RECIST 1.1 were to continue to undergo tumor assessment every 6 weeks from the date of the last tumor assessment, or sooner, if clinically indicated, until disease progression based on RECIST 1.1. Additionally, when a new antitumor treatment was to be initiated more than 4 weeks after the last tumor evaluation, the tumor was to be evaluated as far as possible before the start of the new treatment, and the implementation of the new antitumor treatment was to be recorded in the case report form.

In both the Treatment Period and the Posttreatment Period, the frequency of tumor assessment was permitted to be changed to every 12 weeks after the cutoff date. After progression of the disease, all subjects were to be followed every 12 weeks for survival, unless they withdrew consent or the survival follow-up was terminated by the sponsor for all subjects.

The study set the cutoff date when all subjects had completed their Week 12 or later tumor assessments. The Week 12 assessments were to be performed for subjects who had discontinued treatment earlier than that time unless PD was documented.

Number of Subjects (Planned and Enrolled)
Planned: Approximately 35 subjects with advanced or metastatic STS (1 of 2 subtypes: ADI or LMS) were planned to be entered and treated. At least 5 subjects of them were planned to be entered and treated in each subtype. Up to a maximum of approximately 20 subjects (at least approximately 16 subjects) with advanced or metastatic STS of OTH were to be entered and treated. Thus, the total number of subjects was expected to be at least approximately 51.

Enrolled: 52 subjects were entered and 51 subjects were treated.

Diagnosis and Main Criteria for Inclusion
1. Histologically or cytologically confirmed STS of high or intermediate grade, except the following histological subtypes: embryonal rhabdomyosarcoma, chondrosarcoma, osteosarcoma, Ewing tumors/primitive neuroectodermal tumor (PNET), gastro-intestinal stromal tumor (GIST), dermatofibrosarcoma protuberans, inflammatory myofibroblastic sarcoma, neuroblastoma, malignant mesothelioma, mixed mesodermal tumors of the uterus.
2. Documented evidence of advanced or metastatic (locally recurrent, locally advanced or metastatic) STS, not amenable to surgery or radiotherapy.

3. Radiographic evidence of disease progression by RECIST criteria on or after the last chemotherapy regimen for advanced or metastatic STS within the 6 months before study enrollment.

4. Presence of measurable disease meeting the following criteria: At least 1 lesion of ≥10 mm in long-axis diameter for non-lymph nodes or ≥15 mm in short-axis diameter for lymph nodes which was serially measurable according to RECIST 1.1 using either computed tomography (CT)/magnetic resonance imaging (MRI) or color photography including a ruler. Lesions that have had radiotherapy (RT) must have shown evidence of PD based on RECIST 1.1 to be deemed a target lesion.

5. Subjects should have received at least 1 standard chemotherapy for advanced or metastatic STS (an anthracycline or an ifosfamide monotherapy, or a combination therapy).

6. Aged ≥20 years at the time of informed consent.

7. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1.

8. Adequate bone marrow function:
   a. Absolute neutrophil count (ANC) ≥1.5 × 10^3/μL
   b. Platelet count ≥1.0 × 10^5/μL
   c. Hemoglobin ≥10.0 g/dL

9. Adequate liver function.
   a. Bilirubin ≤1.5 times the upper limit of normal (ULN) except for unconjugated hyperbilirubinemia of Gilbert’s syndrome.
   b. Alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤3 times ULN. For subjects with hepatic metastasis, ≤5 times ULN.

10. Adequate renal function defined as serum creatinine ≤1.5 times ULN and calculated creatinine clearance ≥40 mL/min per the Cockcroft and Gault formula.

   **Cockcroft Gault formula**
   Male: \((\frac{[140 – age] \times weight [kg]}{Serum \ creatinine \ [mg/dL] \times 72}) = XX \ mL/min\)
   Female: \((\frac{[140 – age] \times weight [kg]}{Serum \ creatinine \ [mg/dL] \times 72}) = XX \ mL/min \times 0.85\)

11. All female subjects were considered to be of child-bearing potential unless they were postmenopausal (at least 12 months consecutive amenorrhea, in the appropriate age group and without other known or suspected cause), or have been sterilized surgically (ie, bilateral tubal ligation ≥1 menstrual cycle before study drug administration, or have undergone a hysterectomy and/or bilateral oophorectomy). Female subjects of child-bearing potential were to have agreed to use 2 forms of highly effective contraception from the last menstrual period before study drug administration (or to use a double barrier method as described below until they were on 2 forms of highly effective contraception for at least 1 menstrual cycle), during the study treatment, and for 3 months after the final dose of study treatment. Female subjects exempted from this requirement were subjects who practiced total abstinence. If currently abstinent, the subject was to have agreed to use a double barrier method of contraception, ie, condom and occlusive cap (diaphragm or cervical/vault caps) with spermicide or until they were on 2 forms of highly effective contraception for at least 1 menstrual cycle if they became sexually active during the study treatment and for 3 months after the final dose of study treatment. Highly effective contraception included:
   a. Placement of intrauterine device or system.
   b. Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault cap) with spermicide.
   c. Established hormonal contraceptive methods: oral, injectable or implant. Female subjects who were using hormonal contraceptives must have been on a stable dose of the same hormonal contraceptive product from the last menstrual period before study drug administration, and must have continued to use the same hormonal contraceptive product during study treatment, and for 3 months after the final dose of study treatment.
   d. Vasectomized partner with confirmed azoospermia.
12. Male subjects and their female partner who was of child-bearing potential (as defined in Inclusion 11), who were not practicing total abstinence were to have agreed to use 2 forms of highly effective contraception from the last menstrual period of their female partner before first study drug administration (or to use a double barrier method as described above until they were on 2 forms of highly effective contraception for at least 1 menstrual cycle), during study treatment, and for 3 months after the final dose of study treatment. For subjects who were abstinent, the subject was to have agreed to use a double barrier method of contraception if they became sexually active, or until they were on 2 forms of highly effective contraception as described above.

13. Voluntary agreement to provide written informed consent and the willingness and ability to comply with all aspects of the protocol.

Test Treatment, Dose, Mode of Administration, and Batch Number(s)
Eribulin mesilate 1.4 mg/m² intravenous (IV) given over 2 to 5 minutes on Days 1 and 8 every 3 weeks (21 days).
The lot numbers used during this study were: P93021ZZB, P14022ZZB, and P14023ZZB

Reference Therapy, Dose, Mode of Administration, and Batch Number(s)
No reference therapy was used in this study.

Duration of Treatment
The administration of eribulin mesilate was continued until any 1 of the following treatment discontinuation criteria was met.
1. Documented disease progression including appearance of new lesions according to RECIST 1.1
2. Subject became ineligible after enrollment
3. Life-threatening allergic reaction
4. Unable to resume treatment within 14 days after the planned first administration date of the subsequent cycle
5. Necessary to further reduce the dose to lower than 0.7 mg/m²
6. Pregnancy
7. Subject’s refusal of treatment or withdrawal of consent
8. Unable to comply with the protocol, making it difficult to safety continue in the study as judged by the investigator or subinvestigator
9. Any other condition that makes treatment discontinuation appropriate at the discretion of the investigator or subinvestigator

Assessments
Efficacy
All efficacy assessments other than for OS were performed based on the tumor response evaluations as determined by the investigator (or subinvestigator) and the Independent Review Committee (IRC) according to RECIST 1.1. If there were discrepancies in the tumor response evaluations, the IRC result was used for the primary analysis.
Tumor response was evaluated every 6 weeks during treatment, and was confirmed at least 4 weeks after the first observation of CR or PR. Given the primary endpoint of the study, tumors were evaluated at Week 12 during treatment in all subjects (even if study treatment had been discontinued, unless progression had been previously documented).

Primary Efficacy Variable:
The primary efficacy assessment was the progression-free rate at 12 weeks (PFR_{12wks}): after start of therapy, measured as a binary variable, based on the disease evaluation performed at Week 12 after start of treatment. Subjects were considered a “success” if 1 radiological evaluation performed at least Week 12 after the start of therapy indicates an “SD”, or a “CR” or a “PR” as defined according to the RECIST 1.1; all other cases were considered failures (including disease progression or death before the Week 12 evaluation, or presented
unknown disease status at Week 12). If a new anticancer treatment was started before the Week 12 evaluation, the subject was considered a failure for the primary endpoint.

**Secondary Efficacy Variables:**
Efficacy was further assessed using the following secondary endpoints: progression-free survival (PFS) (defined as the time from the date of first dose of study drug to the first documented date of event [disease progression or death from any cause, whichever occurs first]); OS (defined as the time from the date of first dose of study drug to the date of death from any cause; in the absence of confirmation of death, subjects will be censored either at the date that the patient was last known to be alive or the date of study cutoff, whichever occurred earlier); objective response rate (ORR) (defined as the proportion of subjects who have a best overall response [BOR] of CR or PR); disease control rate (DCR) (defined as the proportion of subjects who have BOR of CR + PR + SD); durable stable disease rate (dSDR) (defined as the proportion of subjects who have the dSD [duration of SD ≥11 weeks]); and clinical benefit rate (CBR) (defined as the proportion of subjects who have BOR of CR + PR + dSD).

**Pharmacokinetics**
The PK parameters including the concentration of eribulin mesilate immediately after administration ($C_{\text{end}}$) and the concentration at 168 h after administration ($C_{168\text{hr}}$) and were calculated in as many treated subjects as possible to evaluate the PK profiles of eribulin mesilate:
Plasma concentration data were obtained from blood samples drawn at Cycle 1 and Cycle 2 at specific time points:
  - Cycle 1 (Day 1: predose, immediately after end of infusion, 168 h after IV administration)
  - Cycle 2 (Day 1: predose, immediately after end of infusion, 168 h after IV administration)

**Safety**
Safety was assessed by monitoring and recording all adverse events (AEs), including all CTCAE version 4.0 grades, and serious AEs (SAEs); regular monitoring of hematology, blood chemistry, and urinalysis values; periodic measurement of vital signs (systolic blood pressure, diastolic blood pressure, pulse rate, body temperature, and body weight); 12-lead electrocardiograms (ECGs); and physical examinations.

**Bioanalytical Methods**
Plasma concentrations of eribulin: liquid chromatography with tandem mass spectrometry (LC-MS/MS) method.

**Statistical Methods**
The following analysis sets were defined for this study:
  - **Full Analysis Set (FAS)** included all subjects who received at least 1 dose of study drug. This was the primary analysis set for all efficacy evaluations.
  - **Per Protocol Set (PPS)** included those subjects who received at least 1 dose of study drug, had no major protocol violation, and had both baseline and postbaseline tumor assessments. Subjects for whom death occurred before the first postbaseline tumor assessment were also included. Full criteria for exclusion from the analysis set were determined and documented before the database lock for the primary analysis of $PFR_{12\text{wks}}$. This was the secondary analysis set for efficacy evaluations.
  - **Safety Analysis Set** included all subjects who received at least 1 dose of the study drug, and had at least 1 postbaseline safety evaluation. This was the analysis set for all safety evaluations.
  - **Pharmacokinetic Analysis Set** included all subjects who received at least 1 dose of the study drug and had sufficient pharmacokinetic data to derive at least 1 pharmacokinetic parameter.
A cutoff date of 14 Nov 2014 was used for data in this study.

**Efficacy Analyses:**
Efficacy analyses were performed primarily on subjects with ADI or LMS, and on subjects with OTH. In addition, efficacy analyses were performed secondarily on all subjects in all strata.
$PFR_{12\text{wks}}$ was presented with associated 1-sided exact 90%, 2-sided exact 90% and 95% confidence intervals (CIs) using the binomial distribution.
PFS and OS were estimated by the Kaplan-Meier method, and estimates of PFS probabilities and OS
probabilities were plotted over time. Estimates of PFS probabilities at 3, 6, 9 and 12 months and OS probabilities at 6, 12, 18, and 24 months were calculated with their 2-sided 95% CIs; median PFS and median OS were provided with 2-sided 95% CIs.

ORR, DCR, CBR, and dSDR were estimated based on the tumor response assessments performed according to RECIST 1.1, and were presented with associated 2-sided exact 95% CI using the binomial distribution.

**Pharmacokinetic Analyses:**
Pharmacokinetic parameters were estimated by plasma eribulin concentrations.

**Safety Analyses:**
Safety analyses were performed for subjects with ADI or LMS, subjects with OTH and for all subjects of the Safety Analysis Set.

The number of subjects who developed AEs after administration of study drug and the incidence rate of AEs were calculated. AEs were summarized by system organ class (SOC), preferred terms (PT), CTCAE Grade, and causal relationship to study drug. Summary statistics (mean, standard deviation, median, minimum, and maximum) were calculated for laboratory values, physical examination, vital signs, 12-lead ECG, and their changes from baseline.

**Sample Size Rationale:**
A total of approximately 35 subjects with advanced or metastatic STS (1 of 2 subtypes: ADI or LMS) were to be registered and treated.

Up to a maximum of approximately 20 subjects (at least approximately 16 subjects) with STS of OTH were to be registered and treated.

The required number of subjects with ADI or LMS was determined based on the 1-sample binomial distribution and the following assumptions: The null hypothesis (H₀): PFR₁₂wks ≤20%; the alternative hypothesis (H₁): PFR₁₂wks ≥40%; 1-sided type I error (α) = 0.05; and power = 80%. The threshold PFR₁₂wks (P₀ = 20%) and the expected PFR₁₂wks (P₁ = 40%) were based on the EORTC’s STBSG report (European Organisation for Research and Treatment of Cancer European Union, Soft Tissue and Bone Sarcoma Group) by Van Glabbeke, et al (2002) and the results of the overseas Phase 2 study E7389-E044-207 (Study 207).

The number of subjects with OTH was determined based on the 1-sample binomial distribution with the threshold PFR₁₂wks (P₀ = 15%) and the expected PFR₁₂wks (P₁ = 35% or 40%). The actual 1-sided α and power when the sample size was from 13 to 22 is shown below. The above assumptions were considered conservative based on the results for subjects with other than ADI or LMS in Study 207.

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<th>Sample Size</th>
<th>Actual 1-sided α</th>
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<td>13</td>
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<td>64.7%</td>
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<td>15</td>
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Thus, the total number of subjects was expected to be at least approximately 51.

**Results**

**Subject Disposition/Analysis Sets**
A total of 55 subjects were enrolled into the study (enrolled subjects include all subjects who signed informed consent forms). Of these 55 subjects, 3 subjects were screening failures and 52 subjects were eligible to continue in the study. Of the 52 subjects who continued into the study, 1 subject did not receive any study drug. A total of 51 subjects received at least 1 dose of study drug. In this study the FAS, PPS, Safety Analysis Set, and PK Analysis Set were assessed for all 51 treated subjects.
Efficacy

- The primary efficacy endpoint of this study was PFR\textsubscript{12wks} in the FAS, and analysis showed that the 2 strata and their total responded to treatment with eribulin mesilate with progression-free survival at Week 12 in 21 of 35 subjects (60.0%, 95% CI: 42.1, 76.1) in the ADI or LMS stratum, 5 of 16 subjects (31.3%, 95% CI: 11.0, 58.7) in the OTH stratum, and 26 of 51 subjects (51.0%, 95% CI: 36.6, 65.2) in total.
- PFS was a secondary endpoint and was assessed at the database cutoff date. The median PFS time was 5.52 months (95% CI: 2.79, 8.18) in the ADI or LMS stratum, 2.01 months (95% CI: 1.22, 4.07) in the OTH stratum, and 4.07 months (95% CI: 2.56, 5.55) in total.
- OS was assessed as a secondary endpoint. A total of 38/51 subjects (74.5%) had died at the database cutoff date (25/35 subjects [71.4%] in the ADI or LMS stratum and 13/16 subjects [81.3%] in the OTH stratum). The median OS was 16.95 months (95% CI: 11.01, 20.47) in the ADI or LMS stratum, 7.64 months (95% CI: 3.84, 16.13) in the OTH stratum, and 13.17 months (95% CI: 9.49, 18.33) in total. The OS rate at 6 months was 82.9% in the ADI or LMS stratum, 68.8% in the OTH stratum, and 78.4% in total. The OS rate at 12 months was 57.1% in the ADI or LMS stratum, 43.8% in the OTH stratum, and 52.9% in total.
- The BOR included no CRs or PRs. The secondary efficacy endpoint of ORR was 0% (0/35 subjects; 95% CI: 0.0, 10.0) in the ADI or LMS stratum, 0% (0/16 subjects; 95% CI: 0.0, 20.6) in the OTH stratum, and 0% (0/51 subjects; 95% CI: 0.0, 7.0) in total.
- The secondary efficacy endpoint of DCR was 80.0% (28/35 subjects; 95% CI: 63.1, 91.6) in the ADI or LMS stratum, 50.0% (8/16 subjects; 95% CI: 24.7, 75.3) in the OTH stratum, and 70.6% (36/51 subjects; 95% CI: 56.2, 82.5) in total.
- The secondary efficacy endpoint of CBR was 74.3% (26/35 subjects; 95% CI: 56.7, 87.5) in the ADI or LMS stratum, 50.0% (8/16 subjects; 95% CI: 24.7, 75.3) in the OTH stratum, and 66.7% (34/51 subjects; 95% CI: 52.1, 79.2) in total.
- The secondary efficacy endpoint of dSDR was 74.3% (26/35 subjects; 95% CI: 56.7, 87.5) in the ADI or LMS stratum, 50.0% (8/16 subjects; 95% CI: 24.7, 75.3) in the OTH stratum, and 66.7% (34/51 subjects; 95% CI: 52.1, 79.2) in total.

Pharmacokinetics

- Plasma concentration data will be pooled for population PK analysis and its results will be provided in a separate report.

Safety

- All 51 treated subjects experienced at least 1 treatment-emergent adverse event (TEAE). Overall, the most common TEAEs (occurring in ≥30% subjects) reported during the study were leukopenia (51/51 subjects [100.0%]), neutropenia (50/51 subjects [98.0%]), lymphopenia (40/51 subjects [78.4%]), anaemia (24/51 subjects [47.1%]), cancer pain (23/51 subjects [45.1%]), nausea, pyrexia (each 21/51 subjects [41.2%]), malaise (20/51 subjects [39.2%]), constipation, and neuropathy peripheral (each 16/51 subjects [31.4%]).
- Overall, 96.1% of subjects (49/51 subjects) had at least 1 TEAE of Grade 3 or above. Overall, the most frequent Grade 3 or above TEAEs were neutropenia (44/51 subjects [86.3%]), leukopenia (38/51 subjects [74.5%]), lymphopenia (17/51 subjects [33.3%]), anaemia (7/51 subjects [13.7%]), hypophosphataemia (5/51 subjects [9.8%]), and febrile neutropenia (4/51 subjects [7.8%]).
- All 51 treated subjects experienced TEAEs that were considered by the investigator to be related (ie, possibly or probably related) to study drug. Overall, the most common treatment-related TEAEs (occurring in ≥30% subjects) reported during the study were leukopenia (51/51 subjects [100.0%]), neutropenia (50/51 subjects [98.0%]), lymphopenia (40/51 subjects [78.4%]), anaemia (24/51 subjects [47.1%]), pyrexia (21/51 subjects [41.2%]), malaise (20/51 subjects [39.2%]), and nausea (19/51 subjects [37.3%]).
- Overall, there was 1 TEAE that led to death in 1 subject in the LMS stratum during the study. The subject died of cardiac failure during the study after receiving 63 days of treatment; the event was reported as an SAE and was considered to be not related to study drug.
• Overall, SAEs were reported in 15/51 (29.4%) subjects; of these 14 subjects reported nonfatal SAEs and 1 subject reported a fatal SAE (cardiac failure). The most common nonfatal SAEs were cancer pain (3/51 [5.9%] subjects).

• Overall, TEAEs that led to withdrawal of study drug were reported in 4/51 (7.8%) subjects. The TEAEs that led to withdrawal of study drug were cardiac failure, infectious pleural effusion, pneumonia, and interstitial lung disease (each in 1/51 [2.0%] subjects).

• Overall, TEAEs that led to study drug dose reduction were reported in 16/51 (31.4%) subjects. The most common TEAE that led to study drug dose reduction was neutropenia (13/51 [25.5%] subjects).

• For hematology parameters, treatment-emergent markedly abnormal laboratory values (TEMAVs) were reported for neutrophils (low; 44/51 [86.3%] subjects), leukocytes (low; 38/51 [74.5%] subjects), lymphocytes (low; 17/51 [33.3%] subjects), and hemoglobin (low; 8/51 [15.7%] subjects). For blood chemistry parameters, the most common TEMAVs were reported for alanine aminotransferase (high; 4/51 [7.8%] subjects), phosphate (low; 4/51 [7.8%] subjects), potassium (low; 3/51 [5.9%] subjects), and glucose (high; 3/51 [5.9%] subjects).

• No meaningful changes from baseline were observed for any of the vital sign parameters (weight, systolic blood pressure, diastolic blood pressure, pulse rate, and body temperature) during the study.

• No trends over time were noted for ECG parameters (QTc corrected by Fridericia’s method [QTcF], heart rate). However, 3 subjects had a QTcF value exceeding 500 msec or the change from baseline in QTcF exceeding 60 msec at 1 post-eribulin mesilate infusion time point. Of these 2 subjects with abnormal QTcF value returned to normal.

• There was little change in ECOG-PS over the course of the study and most subjects remained Grade 0 or Grade 1 throughout.

Conclusions

• The primary efficacy endpoint PFR_{12wks} was 60.0% in the ADI or LMS stratum, 31.3% in the OTH stratum, and 51.0% in total. The median PFS time was 5.52 months in the ADI or LMS stratum, 2.01 months in the OTH stratum, and 4.07 months in total. The median OS was 16.95 months in the ADI or LMS stratum, 7.64 months in OTH stratum, and 13.17 months in total. These data indicate that eribulin mesilate showed clinical activity in previously treated subjects with advanced or metastatic STS.

• TEAEs were mainly hematological. The most common Grade 3 or above TEAEs were neutropenia (86.3%), leukopenia (74.5%), lymphopenia (33.3%), anaemia (13.7%), hypophosphataemia (9.8%), and febrile neutropenia (7.8%). This safety profile was consistent with that observed in previous clinical studies of eribulin mesilate. Eribulin mesilate was generally well tolerated with a predictable safety profile and had a manageable tolerability profile in advanced or metastatic STS.

Date of Report
25 May 2015