SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	to be determined
Name of Active Ingredient	Levofloxacin hydrate (JAN)
Title of Study	A phase III, randomized, parallel-group, confirmatory study of DR-3355 injection in patients with community-acquired pneumonia
Study Centre(s)	87 Study Sites
Publication (reference)	None
Studied Period	Date of obtaining first consent: November 22, 2007 Date of last observation: October 1, 2008
Phase of Development	Phase III
Objectives	To confirm the non-inferiority of the efficacy of DR-3355 injection in patients with community-acquired pneumonia using ceftriaxone sodium hydrate (ceftriaxone sodium, i.e., ceftriaxone) as a control. The safety of DR-3355 injection will also be evaluated.
Methodology	Multicenter, randomized (central registration), open-label (primary efficacy endpoint to be evaluated by a third party (hereinafter referred to as end-point assessment committee) under blinded condition), non-inferiority confirmatory study.
Number of Patients (planned and analyzed)	Planned subjects : 240 (DR-3355inj group: 120, ceftriaxone group: 120) Registered subjects and Randomized subjects: 260 (DR-3355inj group: 136, ceftriaxone group: 124) Analyzed subjects: Safety analysis set:259 (DR-3355inj group: 136, ceftriaxone group: 123) Per protocol set (PPS): 200 (DR-3355inj group: 108, ceftriaxone group: 92)
Diagnosis and Main Criteria for Inclusion	Subjects with community-acquired pneumonia (bacterial pneumonia) who met all of the inclusion criteria, did not fulfill any of the exclusion criteria, and gave written consent (signed) of their own free will were enrolled in the study. (1)Men and women aged 20-79 years at the time of giving informed consent. (2)Patients who developed symptoms diagnosed as bacterial pneumonia outside of the hospital and for whom inpatient treatment was judged necessary by the investigator or

	subinvestigator. (3)Patients who met the following symptoms/findings criteria on the day of or the day before the start of study drug treatment: 1)Presence of acute and new infiltrative shadow identified by chest X-ray or chest CT scanning 2)Body temperature ≥37.0°C (axillary) 3)Patients who met at least one of the two following: i)CRP increased (≥1.0 mg/dL) ii)White blood cell count increased (≥9,000/mm3) 4)Presence of respiratory symptoms such as cough, sputum (purulent sputum), chest pain, and dyspnea, or moist rales.
Test Product, Dose and Mode of Administration, Batch Number	Investigational product (lot No.):DR-3355 inj (060551) Dosage and administration:Intravenous drip infusion of DR-3355 at a dose of 500 mg once daily over 60 minutes.
Duration of Treatment	Intravenous drip infusion of DR-3355 500 mg once daily or ceftriaxone 1 g (potency) twice daily for 7 to 14 days.
Reference Therapy, Dose and Mode of Administration, Batch Number	Comparator (lot No.):Ceftriaxone (Ad3355X0-07T01, Ad3355X0-07T02) Dosage and administration:Intravenous drip infusion of ceftriaxone at a dose of 1 g (potency) twice daily (morning and evening) over 30 minutes after dissolving in the attached solution.
Criteria for Evaluation	【Efficacy endpoints】 Primary endpoint Clinical response at completion/discontinuation of treatment evaluated by the end-point assessment committee (success rate) Secondary endpoints (1)Clinical response at completion/discontinuation of treatment evaluated by the investigator or subinvestigator (success rate) (2)Clinical response on Days 3 and 7 and at the last observation evaluated by the end-point assessment committee (success rate) (3)Microbiologic response at completion/discontinuation of treatment evaluated by the end-point assessment committee (negative conversion rate) (4)Microbiologic response at completion/discontinuation of treatment evaluated by the end-point assessment committee (eradication rate) 【Safety endpoints】

	(1)Incidence of adverse events and of adverse drug reactions (2)Incidence of adverse events and of adverse drug reactions by major background factors (3)Changes in clinical laboratory values
Statistical Method	【Efficacy analysis】 As the primary endpoint, point estimation was obtained for the difference in clinical response (success rate) at completion/discontinuation of treatment evaluated by the end-point assessment committee between the DR-3355inj group and the ceftriaxone group to calculate the two-sided 95% confidence interval based on the normal approximation. When the lower limit of the two-sided 95% confidence interval was ≥-10%, it was judged that non-inferiority of the DR-3355inj group to the ceftriaxone group was confirmed. As secondary endpoints, point estimation and the two-sided 95% confidence interval were calculated for both groups. 【Safety analysis】 The number, the percentage, two-sided 95% confidence interval of subjects with adverse events and adverse drug reactions, and the number of events in each group were shown for the safety analysis set. Tabulation was also conducted for the safety data by system organ class/preferred terms.
Summary - Conclusion	【Results of efficacy】 Primary endpoint: Clinical response at completion/discontinuation of treatment evaluated by the end-point assessment committee (success rate) The success rate at completion/discontinuation of treatment was 88.5% (92/104) in the DR-3355inj group and 88.8% (79/89) in the ceftriaxone group. Because the lower limit of the 95% confidence interval of the intergroup difference exceeded -10%, non-inferiority of DR-3355 to ceftriaxone was confirmed. Secondary endpoints （1） Clinical response at completion/discontinuation of treatment evaluated by the investigator or subinvestigator (success rate) The success rate at completion/discontinuation of treatment was 93.5% (101/108) in the DR-3355inj group and 91.2% (83/91) in the ceftriaxone group.

	（2） Clinical response on Days 3 and 7 and at the last observation (success rate) The success rate on Days 3, 7 and at the last observation evaluated by the end-point assessment committee was 45.2% (47/104), 68.0% (34/50), 88.9% (80/90) in the DR-3355inj group and 33.7% (30/89), 78.0% (32/41), 83.8% (62/74) in the ceftriaxone group, respectively. （3） Microbiologic response at completion/discontinuation of treatment (negative conversion rate) Microbiologic response at completion/discontinuation of treatment evaluated by the end-point assessment committee (negative conversion rate) was 96.7% (59/61) in the DR-3355inj group and 97.8% (44/45) in the ceftriaxone group. （4） Microbiologic response at completion/discontinuation of treatment (eradication rate) Microbiologic response of the pathogen evaluated by the end-point assessment committee (eradication rate) was 97.2% (69/71) in the DR-3355inj group and 98.0% (50/51) in the ceftriaxone group. 【Results of safety】 Incidence of adverse events was 72.8% (99/136, 340 events) in the DR-3355inj group and 71.5% (88/123, 275 events) in the ceftriaxone group. The incidence of adverse drug reactions was 53.7% (73/136, 223 events) in the DR-3355inj group and 56.9% (70/123, 150 events) in the ceftriaxone group. 【Conclusions】 The clinical response at completion/discontinuation of treatment (success rate) of the DR-3355inj group was 88.5% (92/104). Because the lower limit of the 95% confidence interval of the intergroup difference with the ceftriaxone group exceeded -10%, non-inferiority of DR-3355 to ceftriaxone was confirmed. No clinically relevant safety problems were observed with DR-3355 injection. Intravenous administration of DR-3355 500 mg once daily for 7 to 14 days is therefore considered to demonstrate sufficient therapeutic effect for community-acquired pneumonia (bacterial pneumonia) in adults.
Date of Report	Jun 1, 2010