SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	CRAVIT ® INTRAVENOUS DRIP INFUSION
Name of Active Ingredient	Levofloxacin
Title of Study	Comparative study of DR-3355 injection and pazufloxacin injection in patients with urinary tract infection
Investigators	
Study Centre(s)	61 sites
Publication (reference)	None
Studied Period	Date of obtaining first consent: May, 2012 Date of last observation: February, 2014
Phase of Development	Phase 3
Objectives	The purpose of this study is to compare the bacteriological efficacy and safety of DR-3355 injection and pazufloxacin (PZFX) injection on urinary tract infection at the end of intravenous treatment, and to verify the non-inferiority of DR-3355 injection to PZFX injection. Additionally, the efficacy and safety is evaluated after switching from DR-3355 injection to levofloxacin (LVFX) oral agent.
Methodology	Open-label, multicentre, randomized study
Number of Patients (planned and analyzed)	Planned: 324 patients Registered: 325 patients (DR-3355 group: 162 patients, PZFX group: 163 patients) Analyzed: Per protocol set (PPS): 252 patients (DR-3355 group: 127 patients, PZFX group: 125 patients) Evaluation of safety: 324 patients (DR-3355 group: 162 patients, PZFX group: 162 patients)
Diagnosis and Main Criteria for Inclusion	Diagnosis: Urinary tract infection (acute uncomplicated pyelonephritis, complicated pyelonephritis, complicated cystitis) Inclusion: 1) Patients between the ages of 20 to 79 at the time of obtaining informed consents. 2) Patients who require hospitalization at the time of enrollment. 3) Patients with symptoms of pyelonephritis or cystitis. 4) Patients who meet the criteria for pyuria and have bacteria in the urine 5) Patients who require an injection treatment.(any of the following symptoms: temperature of 38°C or more, nausea or vomiting, dehydration, suspicion of bacteremia, urine flow disorder, anorexia, diarrhea)
Test Product, Dose and Mode of Administration, Batch Number	Test product (batch number): DR-3355 injection (D3355I0H11T01A) Oral LVFX (D3355F0S11T01A) Dosage and administration: Intravenous administration of DR-3355inj at 500 mg, once daily Oral administration of LVFX at 500 mg, once daily
Duration of Treatment	Intravenous therapy for 5 days could be followed by LVFX for 5 days.
Reference Therapy, Dose and Mode of Administration, Batch Number	Control drug (batch number): PZFX injection (D3355I0H11T02A) Oral LVFX (D3355F0S11T01A) Dosage and administration: Intravenous administration of PZFX inj at 500 mg, twice daily

	Oral administration of LVFX at 500 mg, once daily
Criteria for Evaluation	Primary endpoint: Bacteriological efficacy at the end of intravenous treatment (PPS) Secondary endpoint: Clinical efficacy at the end of intravenous treatment (PPS) Clinical efficacy and bacteriological efficacy at the test of cure Clinical efficacy and bacteriological efficacy at the evaluation of recurrence Bacteriological response by causative bacteria Antipyretic potency
Statistical Method	As the primary endpoint, the point estimate and the two-sided 95% confidence interval (CI) based on the normal approximation were estimated for the difference in bacteriological efficacy between the DR-3355 group and the PZFX group at the end of intravenous treatment. When the lower limit of the two-sided 95% CI was above −10%, it was judged that non-inferiority of the DR-3355 group to the PZFX group was confirmed.
Summary - Conclusion	Efficacy summary: The bacteriological efficacy rate at the end of intravenous treatment was 93.7% (119/127, 95% CI: 89.5 to 97.9) in the DR-3355 group, 89.5% (111/124, 95% CI: 84.1 to 94.9) in the PZFX group, and the between-group difference was 4.2% (95% CI: −2.7 to 11.0). The lower limit of 95% CI of the between-group difference was above the non-inferiority margin (−10%), non-inferiority of DR-3355 versus PZFX was confirmed. Switch therapy from DR-3355 injection to LVFX oral agent showed the comparable therapeutic effect in switch therapy from PZFX injection to LVFX oral agent. Safety summary: The incidence of adverse events up to the end of intravenous treatment was 44.4% (72/162, 95% CI: 36.8 to 52.1) in the DR-3355 group, 45.1% (73/162, 95% CI: 37.4 to 52.7) in the PZFX group. The between-group difference was −0.6% (95% CI: −11.4 to 10.2), no clinically significant difference was observed between the groups. The incidence of adverse drug reactions up to the end of intravenous treatment was 30.2% (49/162, 95% CI: 23.2 to 37.3) in the DR-3355 group, 26.5% (43/162, 95% CI: 19.7 to 33.3) in the PZFX group. The between-group difference was 3.7% (95% CI: −6.1 to 13.5), no clinically significant difference was observed between the groups. There was no difference in the type and incidence of adverse events by severity, adverse event that led to withdrawal between the groups. No adverse events that were considered related to the study drug reported among the serious adverse events in the both groups. Conclusion: From these results, DR-3355 injection is useful for treatment of acute uncomplicated pyelonephritis, complicated pyelonephritis, or complicated cystitis, and there is no important problem in the safety.
Date of Report	December, 2014