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	Clinical trial of DR-3355 injection in patients with gynecological infection
Investigators	
Study Centre(s)	9 sites
Publication (reference)	None
Studied Period	Date of obtaining first consent: July, 2012 Date of last observation: October, 2013
Phase of Development	Phase 3
Objectives	To evaluate the efficacy and safety in patients with gynecological infection receiving a dose of 500 mg DR-3355 injection once a day. To confirm the utility of switching therapy from DR-3355 injection to levofloxacin oral agent.
Methodology	Multicenter, Open-label study
Number of Patients (planned and analyzed)	Planned: 30 patients (As the patient that a bacteriological evaluation is possible: more than 15 subjects) Registered: 23 patients Analyzed: Analysis set of efficacy (PPS) 19 subjects Analysis set of bacteriological efficacy 18 subjects Analysis set of PK 8 subjects Analysis set of safety 22 subjects
Diagnosis and Main Criteria for Inclusion	Diagnosis: intrauterine infection, uterine adnexitis Inclusion criteria: 1) Patients with age of 18 or older at the time of obtaining informed consents 2) Inpatients or outpatients 3) Patients who meet the following criteria and have diagnosis of intrauterine infection or uterine adnexitis a) Patients who have a fever of over 37.0°C b) Patients who have lower abdominal pain (spontaneous pain or pressure pain) c) Patients who have at least one of the following - white blood cell count increase - C-reaction protein (CRP) level increase - presence of purulent vaginal discharge or secretory fluid - presence of pelvic abscess confirmed by an imaging test 4) Patients with 14 points or more of clinical symptoms score Exclusion criteria: 1) Pregnant or breastfeeding patients, patients who have the possibility of being pregnant or patients who hope for cyesis in the study drug exposure period 2) Patients with a history of allergy or dermatological disorder to quinolone antibacterial agents. 3) Patients with severe nervous system disorder, severe cardiac impairment, severe hepatic impairment, or severe renal impairment 4) Patients with infections caused by single pathogens which are known to be resistant or ineffective to the study drug. 5) Patients administrated other antibacterial drugs within 7 days prior

	to the start of the test drug, and whose symptoms have shown improvement. 6) Patients who have received levofloxacin, azithromycin, or other antibacterial drugs (more than twice, except clinical failure patients) within 7 days prior to the start of test drug administration. 7) Patients who require prohibited concomitant medications in this study. 8) Patients who participated in any other clinical trials within the previous 30 days. 9) Patients who have participated in the clinical trial of DR-3355 injection previously, and have been treated with the test drug. 10) Patients who are judged to be inappropriate by the investigator.
Test Product, Dose and Mode of Administration, Batch Number	Test product (batch number): DR-3355 injection (D3355I0H11T01A) Oral levofloxacin (D3355F0S11T01A) Dosage and administration: - Intravenous administration of DR-3355 injection at 500 mg, once a day - Oral administration of levofloxacin at 500 mg, once a day
Duration of Treatment	Three to fourteen days DR-3355 injection (500 mg once daily for 60 min) was continuously administered at least three days, with a switchover from intravenous to oral levofloxacin (500 mg once daily) at the discretion of the investigator in accordance with clinical symptoms.
Reference Therapy, Dose and Mode of Administration, Batch Number	None
Criteria for Evaluation	Primary endpoint: Clinical efficacy at the test of cure (TOC) Secondary endpoint: - Clinical efficacy and bacteriological efficacy at the end of treatment (EOT) - Bacteriological efficacy at the test of cure (TOC)
Statistical Method	The point estimate of the efficacy rate and the two-sided 95% confidence interval were calculated by diagnosis.
Summary - Conclusion	Efficacy summary: The rate of clinical efficacy at TOC in the intrauterine infection and uterine adnexitis patients was 85.7% (6/7) and 80.0% (8/10), respectively. The rate of bacterial eradication rate at TOC in the intrauterine infection and uterine adnexitis patients was 85.7% (6/7) and 63.6% (7/11), respectively. The patients of switchover from intravenous to oral agent in the intrauterine infection and uterine adnexitis patients was 71.4% (5/7),75.0% (9/12), respectively. Except for 1 patient in the uterine adnexitis, those patients were improvement all. The vaginal discharge/plasma drug concentration ratio at two to six hours after end of treatment of DR-3355 injection was 1.46. Safety summary: The incidence of adverse events was 76.2% (16/21) up to the TOC, and 57.1% (12/21) up to the end of intravenous treatment. The incidence of adverse drug reactions was 38.1% (8/21) up to the TOC, and 23.8% (5/21) up to the end of intravenous treatment. Conclusion:

	From these results, DR-3355 injection is useful for treatment of intrauterine infection and uterine adnexitis, and there is no important problem in the safety. In addition, it was confirmed the utility of switching therapy from DR-3355 injection to levofloxacin oral agent.
Date of Report	January 23, 2015