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 peritonitis
Investigators	
Study Centre(s)	14 sites
Publication (reference)	None
Studied Period	Date of obtaining first consent: August, 2012 Date of last observation: October, 2013
Phase of Development	Phase 3
Objectives	To evaluate the efficacy and safety in patients with peritonitis receiving a dose of 500 mg DR-3355 injection once a day.
Methodology	Multicenter, Open-label study
Number of Patients (planned and analyzed)	Planned: 20 patients (As the patient that a bacteriological evaluation is possible: more than 10 subjects) Registered: 21 patients Analyzed: Analysis set of efficacy (PPS) 19 subjects Analysis set of bacteriological efficacy 14 subjects Analysis set of PK 4 subjects Analysis set of safety 21 subjects
Diagnosis and Main Criteria for Inclusion	Diagnosis: peritonitis (including peritonitis caused by pelvic inflammatory disease) Inclusion criteria: 1) Patients with age of 20 or older at the time of obtaining informed consents 2) Inpatients 3) Patients who suffer intra-abdominal infections clinically demonstrated by the inflammatory, abdominal or imaging findings, and who meet any of the following criteria. a) Patients who are to undergo percutaneous drainage of infectious focus, or had received such treatment within 24 hours. However, patients with PID whose treating physicians do not perform drainage at their discretion can be also selected as the subjects. b) In the case of postoperative infection, patients who are confirmed to have gastrointestinal tract fluid or purulent exudate from the drains left during surgery. 4) Initial treatment patients or clinical failure patients with other antimicrobial drugs. 5) Patients that the investigator can obtain a sample from for bacteriological Exclusion criteria: 1) Traumatic injury or operative procedure within 12 hours of sustaining a perforation during lower gastrointestinal tract endoscopy 2) Surgery within 24 hours due to ruptured gastroduodenal ulcer 3) Patients who are managed by open peritoneal drainage 4) Uncomplicated appendicitis, necrotizing pancreatitis, infectious mononucleosis, cystic fibrosis, spontaneous bacterial peritonitis, anaerobe's feeding pathophysiology upon significant role is

	expected 5) Patients who are yet to receive appropriate treatment such as drainage, despite that obvious abscess formation from perforative peritonitis has been confirmed from diagnostic imaging 6) Patients whose IAI symptoms are improving because of surgical intervention including drainage 7) Pregnant or breastfeeding patients, patients who have the possibility of being pregnant or patients who hope for cyesis in the study drug exposure period 8) Patients with a history of allergy or dermatological disorder to quinolone antibacterial agents. 9) Patients with severe nervous system disorder, severe cardiac impairment, severe hepatic impairment, or severe renal impairment 10) Patients with infections caused by single pathogens which are known to be resistant or ineffective to the study drug. 11) Patients administrated other antibacterial drugs within 7 days prior to the start of the test drug, and whose symptoms have shown improvement. 12) 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. 13) Patients who require prohibited concomitant medications in this study. 14) Patients who participated in any other clinical trials within the previous 30 days. 15) Patients who have participated in the clinical trial of DR-3355 injection previously, and have been treated with the test drug. 16) 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) Dosage and administration: Intravenous administration of DR-3355 injection at 500 mg, once a day
Duration of Treatment	Three to fourteen days
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.
Summary - Conclusion	Efficacy summary: The rate of clinical efficacy and bacteriological efficacy at TOC in the peritonitis patients was 70.6% (12/17) and 66.7% (6/9), respectively. The rate of clinical effect at TOC in patients that anaerobic bacteria was found was 47.1% (8/17). In particularly, the rate of clinical efficacy of the patients whom Bacteroides species was found was 33.3% (2/6). The peritoneal exudate/plasma drug concentration ratio at six to eight hours after end of treatment of DR-3355 injection was 1.95.

	Safety summary: The incidence of adverse events was 71.4% (15/21), and the incidence of adverse drug reactions was 28.6% (6/21). Conclusion: From these results, DR-3355 injection is useful for treatment of peritonitis (including peritonitis caused by pelvic inflammatory disease), except case that anaerobe get involved an important role in pathologic condition of peritonitis, and there is no important problem in the safety.
Date of Report	January 23, 2015