SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	NARUVEIN® INJECTION
Name of Active Ingredient	hydromorphone hydrochloride (INN)
Title of Study	DS-7113b injection phase II/III study A DS-7113b injection open clinical study in patients with cancer pain (continuous subcutaneous injection)
Investigators	-
Study Centre(s)	11sites
Publication (reference)	
Studied Period	January 2015 – February 2016
Phase of Development	Phase II/III
Objectives	To evaluate the safety, efficacy and pharmacokinetics following continuous-administration treatment of DS-7113b injection in patients with cancer pain on opioid analgesics, patients with cancer pain without opioid analgesics.
Methodology	A multicenter, open-label, uncontrolled study
Number of Patients (planned and analyzed)	Planned: 20 subjects Analyzed: 21 subjects
Diagnosis and Main Criteria for Inclusion	Inclusion: ・ Patients with cancer pain who have been receiving regular strong opioids for at least 7 days prior to enrollment (Opioid-use group) ・ Patients with cancer pain who have not been on opioid analgesics, whose Pain Intensity is moderate or severe and VAS is 35 mm and over and judged necessary to be treated with strong opioid analgesics (Opioid-naïve group) ・ Patients with an ECOG Performance Status (PS) is ≤ 3, etc. Exclusion: ・ Patients with symptom(s)/finding(s) falling under the contraindications or relative contraindications stated in the package insert for morphine and oxycodone hydrochloride preparations. ・ Patients with serious hepatic, renal, or respiratory disorder, etc.
Test Product, Dose and Mode of Administration, Batch	Test product (batch number): DS-7113b injection 2 mg/1mL（D7113I1H14M01B）

Number	DS-7113b injection 20 mg/2mL（D7113I1H14M05A） Dosage and Administration: ・Opioid-use group: The daily dose of the opioid analgesic in the previous treatment is converted to the morphine injection equivalent dose, and 1/8 dose (±20%) is continuously administered subcutaneously. ・Opioid-naïve group: Received continuous subcutaneous doses of 0.5 to 1.0 mg daily. When it was judged that a dose increase or reduce was necessary during the period of study drug administration, it was possible to increase or reduce the dose step by step.
Duration of Treatment	Treatment period: up to 28 days Post-treatment observation period: 1 day
Reference Therapy, Dose and Mode of Administration, Batch Number	None
Criteria for Evaluation	Efficacy: Pain control rate Definition of Pain control: If the condition that meets all of the following conditions continues for 2 days until Day 7 of administration. 1) The daily dose of DS-7113b is same. 2) Pain intensity is "none" or "mild". 3) Rescue medication less than 4 times a day.) Safety: Adverse event, Clinical laboratory evaluation, etc.
Statistical Method	Efficacy: Pain control rate and its 95% CI were calculated at evaluate point.
Summary - Conclusion	・ The pain control rate at FAS was 85.7% (18/21). (95%CI = 63.7, 97.0) ・ Rescue medication was evaluated by pain relief (PR) score after 10 minutes rescue administration. As a result, "0. None" was 13.2% (9/68), and "1. Slight" or more was 86.8% (59/68). ・ The average value (standard deviation) of the total body clearance in steady state was 61.2 (23.2) L / h. ・ Adverse events observed 33.3% (7/21). The main events (expression rate 5% or more) was somnolence 28.6% (6/21). As described above, DS-711b injection was confirmed to be safe and effective continuous use as a regular treatment with a strong

	opioid analgesic in patients with cancer pain.
Date of Report	October, 4, 2018