

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 intravenous injection)
Investigators	-
Study Centre(s)	35sites
Publication (reference)	-
Studied Period	January 2015 – January 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: 70 subjects Analyzed: 69 subjects
Diagnosis and Main Criteria for Inclusion	<p>Inclusion:</p> <ul style="list-style-type: none"> <li>• Patients with cancer pain who have been receiving regular strong opioids for at least 7 days prior to enrollment (Opioid-use group)</li> <li>• 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)</li> <li>• Patients with an ECOG Performance Status (PS) is ≤ 3, etc.</li> </ul> <p>Exclusion:</p> <ul style="list-style-type: none"> <li>• Patients with symptom(s)/finding(s) falling under the contraindications or relative contraindications stated in the package insert for morphine and oxycodone hydrochloride injections.</li> <li>• Patients with serious hepatic, renal, or respiratory disorder, etc.</li> </ul>
Test Product, Dose and Mode of Administration, Batch	Test product (batch number): DS-7113b injection 2 mg/1mL (D7113I1H14M01A)

Number	<p>DS-7113b injection 20 mg/2mL (D7113I1H14M04A)</p> <p>Dosage and Administration:</p> <ul style="list-style-type: none"> <li>• 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 (<math>\pm 20\%</math>) is continuously administered subcutaneously.</li> <li>• Opioid-naïve group: Received continuous intravenous doses of 0.5 to 1.0 mg daily.</li> </ul> <p>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.</p>
Duration of Treatment	<p>Treatment period: up to 28 days</p> <p>Post-treatment observation period: 1 day</p>
Reference Therapy, Dose and Mode of Administration, Batch Number	None
Criteria for Evaluation	<p>Efficacy: Pain control rate (primary endpoint)</p> <p>Definition of Pain control: If the condition that meets all of the following conditions continues for 2 days until Day 7 of administration.</p> <ol style="list-style-type: none"> <li>1) The daily dose of DS-7113b is same.</li> <li>2) Pain intensity is "none" or "mild".</li> <li>3) Rescue medication less than 4 times a day.</li> </ol> <p>Safety: Adverse event, Clinical laboratory evaluation, etc.</p>
Statistical Method	<p>Primary endpoint:</p> <p>Pain control rate and its 95% CI were calculated at evaluate point.</p>
Summary - Conclusion	<ul style="list-style-type: none"> <li>• The pain control rate at FAS was 73.9% (51/69). (95%CI = 61.9, 83.7)</li> <li>• Rescue medication was evaluated by pain relief (PR) score after 10 minutes rescue administration. As a result, "0. None" was 19.9% (37/186), and "1. Slight" or more was 80.1% (149/186).</li> <li>• The average value (standard deviation) of the total body clearance in steady state was 51.3 (17.4) L / h.</li> <li>• Adverse events observed 40.0%. The main events (expression rate 5% or more) were somnolence 20.0% (14/70), nausea 10.0% (7/70), constipation 7.1% (5/70), and vomiting 7.1%</li> </ul>

	(5/70). 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