SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	NARURAPID® TABLETS
Name of Active Ingredient	hydromorphone hydrochloride (INN)
Title of Study	DS-7113b phase II study A DS-7113b potency ratio assessment study in patients with cancer pain
Investigators	-
Study Centre(s)	38 sites
Publication (reference)	
Studied Period	July 2013 - December 2014
Phase of Development	Phase 2
Objectives	To verify the potency ratio of DS-7113b to morphine, based on the pain control achievement rates following treatment switch to DS-7113b tablets from oral morphine in patients under cancer pain management. Also, to confirm the efficacy and safety of the therapy
Methodology	A multicenter, randomized, double-blind, parallel-group study
Number of Patients (planned and analyzed)	Planned:70 subjects Analyzed:70 subjects
Diagnosis and Main Criteria for Inclusion	Inclusion: ・ Patients with cancer pain whose pain is controlled by 60 mg/day or 90 mg/day of an oral morphine steadly during the screening period. ・ Patients whose frequency of rescue dose during the screening period is two or less. ・ Patients with an ECOG PS of ≤ 3, etc. Exclusion: ・ Patients with serious hepatic, renal, or respiratory disorder. ・ Patients with symptom(s)/finding(s) falling under the contraindications or relative contraindications stated in the package insert of oral morphine preparations, etc.
Test Product, Dose and Mode of Administration, Batch Number	Test product (batch number): DS-7113b tablet 1 mg（D7113T1H12T05） DS-7113b tablet 1.25 mg（D7113T1H12T08） DS-7113b tablet 2 mg（D7113T1H12T06）

<table>
<tr><td></td><td>Dosage and Administration:
The daily dose of each group is as shown in the table below, depenging on their oral morphine dose during the pre-treatment observation period.<table><tr><th rowspan="2">Groups</th><th colspan="2">Daily dose</th></tr><tr><th>Morphine 60mg/day</th><th>Morphine 90mg/day</th></tr><tr><td>Conversion ratio 1:5 group</td><td>12 mg</td><td>18 mg</td></tr><tr><td>Conversion ratio 1:8 group</td><td>7.5 mg</td><td>12 mg</td></tr></table>The study drug was administered until pain control was achieved or for 5 days, whichever was shorter. The study drug was orally administered six times daily in both groups.</td></tr>
<tr><td>Duration of Treatment</td><td>Pre-treatment obsevation period: 3 days
Treatment period: 5 days
Post-treatment obsevation period: 2 days</td></tr>
<tr><td>Reference Therapy, Dose and Mode of Administration, Batch Number</td><td>None</td></tr>
<tr><td>Criteria for Evaluation</td><td>Efficacy: Pain control ratio (Primary endpoint)
Safety: Adverse event, Clinical laboratory evaluation</td></tr>
<tr><td>Statistical Method</td><td>Primary endpoint:
The pain control ratio and its 95% confidence interval (CI) for each group were calculated. Fisher’s exact test was used to compare the pain control ratio between groups, and the difference in the pain control ratio (conversion ratio 1:5 group − conversion ratio 1:8 group) and its 95% CI (two-sided, normal approximation) were calculated.</td></tr>
<tr><td>Summary - Conclusion</td><td>・ The pain control ratio in the FAS was 83.3% in the conversion ratio 1:5 group and 95.0% in the conversion ratio 1:8 group, with a high pain control ratio achieved in both groups.
・ The incidence of adverse events was 46.7% in the conversion ratio 1:5 group and 58.5% in the conversion ratio 1:8 group, showing no significant intergroup difference.
・ Successful pain control was achieved by switching from morphine to hydromorphone with a conversion ratio of 1:5 or 1:8 in Japanese cancer patients who had achieved pain control with oral morphine, with no significant difference between groups. No intergroup difference was observed in the</td></tr>
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	incidence of adverse events or serious adverse events. A conversion ratio between 1:5 and 1:8 is considered clinically appropriate for a switch from morphine to hydromorphone for pain control in cancer patients.
Date of Report	March 26, 2018