Summary of Clinical Study Results for General Audience
Plain Language Summary

1. STUDY NAME

A phase 2a study of S-637880 in patients with neuropathic low back pain

2. WHO SPONSORED THIS STUDY?

This study was sponsored by Shionogi & Co., Ltd.

3. GENERAL INFORMATION ABOUT THIS STUDY

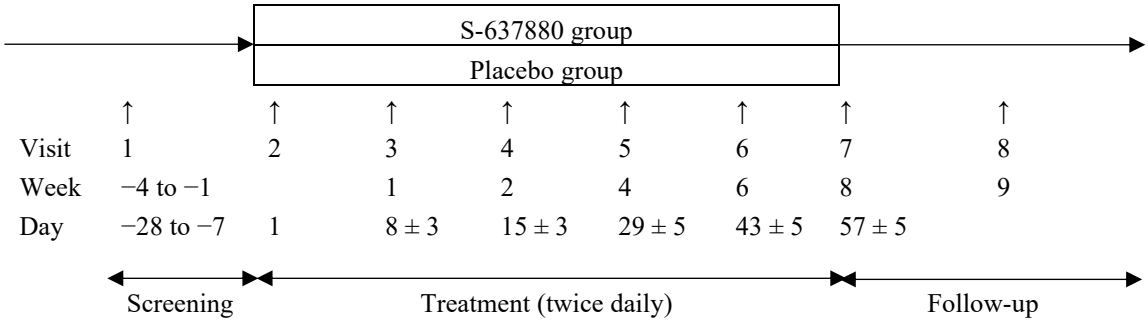
Low back pain is sometimes associated with neurological symptoms such as the pain in the lower limbs caused by intervertebral disc herniation, spinal canal stenosis, lumbar spondylolisthesis, and other conditions. This is called neuropathic pain and may involve burning pain, tingling sensation, or increased sensitivity to touch or low temperature. This type of low back pain is difficult to treat and tends to become chronic (persisting for 3 months or more). This puts limitations on daily activities due to pain, substantially damaging the quality of life of patients with neuropathic low back pain (NLBP). Currently, there are no drugs available for NLBP with a sufficient analgesic effect, and it cannot be said at present that drug therapy has been established. S-637880 was expected to exert a sufficient analgesic effect on NLBP.

This study was a Phase 2 study. Phase 2 studies are usually conducted in a small number of patients to evaluate the desired effects (efficacy) and safety of a drug and to determine the optimal usage of the drug. This study was conducted in a “double-blind” manner. That means that neither the patients nor the study doctors knew who received S-637880 and who received placebo during this study. A placebo used in this study looked like S-637880 but contained no active ingredients. Not letting doctors and patients know which drug the patients are taking is thought to help avoid treatment bias to make a fair evaluation of the study results. Patients in this study were randomized into either the S-637880 group or placebo group so that the age, sex, health condition, etc. were balanced between the groups.

The primary objective of the study was to evaluate the analgesic effect in NLBP patients receiving S-637880 compared with those receiving placebo. The analgesic effect was evaluated by rating the intensity of pain with numbers using a scale called the Numerical Rating Scale (NRS). The change in leg pain from baseline after 8 weeks of treatment with S-637880 is compared with placebo. Patients were asked to rate the daily maximum intensity of pain in their legs from 11 levels ranging from 0 (no pain) to 10 (worst pain imaginable). The safety and pharmacokinetics of S-637880 were also investigated. Pharmacokinetics refers to the time course of a drug in the blood from its absorption by the body until its disappearance from the body.

An outline of the study schedule is shown in Figure 1. The schedule consisted of 3 periods (10 to 13 weeks in total): the screening (1 to 4 weeks), treatment (8 weeks), and follow-up (1 week) periods. The screening period was to examine whether patients were eligible for the study. Then, S-637880 or placebo was administered to the eligible patients twice daily during the 8-week treatment period for evaluating efficacy, safety, and pharmacokinetics. In the follow-up period, post-treatment efficacy and safety were investigated (no study drugs were given in this period).

Figure 1 Study Schedule Outline



This study was conducted in Japan. Although the study was started in March 2021, it was stopped early in September 2021 because patients treated with S-637880 experienced adverse reactions that required study discontinuation (premature discontinuation). An adverse reaction is a medical problem considered by the study doctor to be possibly caused by a drug or treatment used in this study. The adverse reactions that required premature discontinuation of the patient from the study were agranulocytosis (absence of granulocytes, which is a type of white blood cell in the blood) and white blood cell count decreased observed in 1 patient each. The study was discontinued to ensure the safety of patients.

4. WHAT PATIENTS WERE INCLUDED IN THIS STUDY?

This study enrolled patients with neuropathic low back pain (NLBP) who had chronic pain in the legs that was more intense than the low back pain in either or both of the legs and whose low back pain was not attributed to a particular disease (tumor, spondylitis, etc.).

A total of 51 Japanese patients with NLBP took part in this study, with 25 assigned to the S-637880 group (10 men and 15 women, mean age 57.0 years) and 26 assigned to the placebo group (13 men and 13 women, mean age 60.7 years). In consideration of the above-mentioned adverse reactions in the two patients, a total of 30 of the 51 patients (17 in the S-637880 group and 13 in the placebo group) discontinued the study before completing the 8-week study treatment. The reason for discontinuation was study termination (14 in the S-637880 group and 11 in the placebo group), withdrawal by subject (1 in the S-637880 group and 2 in the placebo group), and adverse event (2 in the S-637880 group).

5. WHICH DRUGS WERE STUDIED?

The study drugs used in this study are shown below:

- S-637880
- Placebo (a dummy treatment)

The patients took either S-637880 20 mg or placebo twice daily for 8 weeks.

6. WHAT WERE THE OVERALL RESULTS OF THIS STUDY?

Pain in the legs was rated for the daily worst pain using the Numerical Rating Scale (NRS). The mean scores before starting study treatment were 7.022 and 6.761 in the S-637880 and placebo groups, respectively, compared with 5.395 and 5.527 after 8 weeks of treatment, respectively. The mean differences in scores between before and after 8 weeks of treatment were −1.692 in the S-637880 group and −1.458 in the placebo group.

Because this study was stopped early, the research objectives to be evaluated could not be adequately investigated and only the primary result is mentioned in this section.

7. WHAT WERE THE ADVERSE REACTIONS?

A lot of research is needed to know whether a drug causes a medical problem. So, when new drugs are being investigated researchers keep track of all medical problems (adverse events) that patients have while they are in this study.

This section shows adverse events considered by the study doctor as related to treatment, which are called adverse reactions. One should note that no single clinical study can give a definitive picture of the risks of a drug.

- An “adverse event” means any medical problem that is recorded whether or not it might be caused by the treatment taken.
- An “adverse reaction” means any medical problem or “adverse event” that is considered by the study doctor to be possibly caused by a drug or treatment used in this study.
- A “serious adverse reaction” means an adverse reaction when it is life-threatening, causes lasting problems or needs hospital care.

No patients died during this study.

Adverse reactions requiring premature discontinuation were agranulocytosis and white blood cell count decreased observed in 1 patient each. Agranulocytosis was reported as a serious adverse reaction because the patient was hospitalized. However, this agranulocytosis was resolved with treatment.

The table below shows the serious adverse reaction experienced by patients while taking part in this study.

Serious Adverse Reaction	Number of Patients	
	S-637880 (N=25)	Placebo (N=26)
Agranulocytosis	1 (4.0%)	0

The table below shows the adverse reactions experienced by patients while taking part in this study.

Adverse Reaction	Number of Patients	
	S-637880 (N=25)	Placebo (N=26)
Agranulocytosis	1 (4.0%)	0
White blood cell count decreased	1 (4.0%)	0
Blood glucose increased	0	1 (3.8%)
Urinary occult blood positive	0	1 (3.8%)

8. HOW HAS THIS STUDY HELPED PATIENTS AND RESEARCHERS?

Because this study was stopped early, the research objectives to be evaluated could not be adequately investigated.

9. ARE THERE PLANS FOR FURTHER STUDIES?

No studies of S-637880 are currently ongoing or planned.

10. WHERE CAN I FIND MORE INFORMATION ABOUT THIS STUDY?

This study was sponsored by Shionogi & Co., Ltd.

More information on the study will be posted on the following websites. You can find the information by accessing the website and entering the identifier.

Website	URL	Identifier
Shionogi & Co., Ltd.	English: https://www.shionogi.com/global/en/innovation/randd/clinical-development/clinical-trial-data/clinical-trial01.html Japanese: https://www.shionogi.com/jp/ja/innovation/rd/clinical-development/clinical-trial-data/clinical-trial01.html	Protocol No.: 2004VA421
jRCT	Japanese:	number of clinical trial plan:

Website	URL	Identifier
	https://jrct.mhlw.go.jp/latest-detail/jRCT2031200418	jRCT2031200418