Scilex SP-102 (SEMDEXA)

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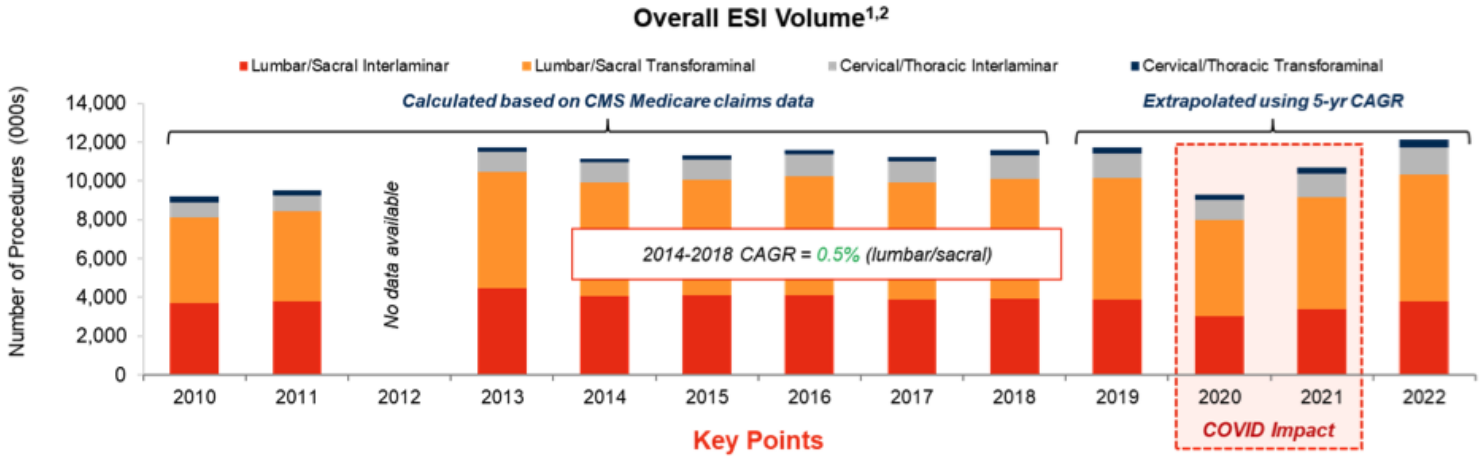
Disclosures

- None

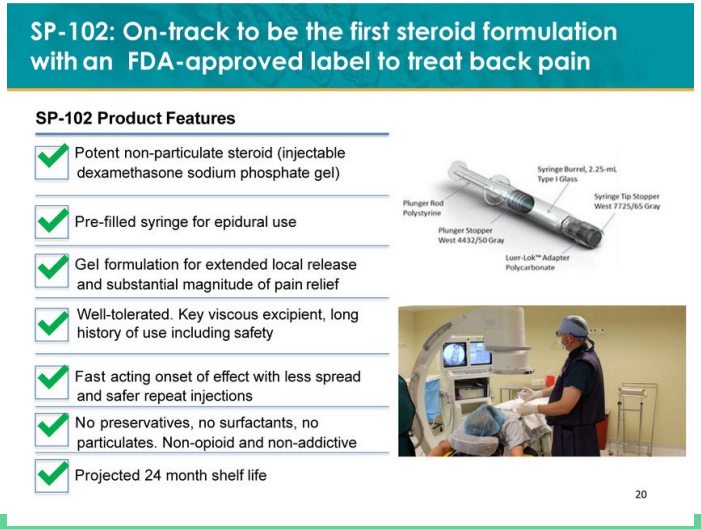
Background

- **US:** 50 million + patients with chronic pain
- **Global:** 1 billion + patients
- An increase need for non opioids solutions for pain relief given the opioid pandemic
- Over 12 million ESI procedures yearly in the US with 88% done for lumbar radiculopathy
- Currently, no product including currently used ESIs approved for epidural use to treat sciatica with safety warnings restricting use



SP-102 (SEMDEXA)

- Non opioid novel injectable corticosteroid gel formulation product (preservative, surfactant, and particulate free) developed for the treatment of radicular pain
- 10 mg dexamethasone sodium phosphate in a viscous gel solution



Corticosteroid Lumbar Epidural Analgesia for Radiculopathy (C.L.E.A.R.) Trial

- **Design:** Phase Ⅲ - multicenter, randomized, double-blind, placebo-controlled study
- **Enrollment:** 401 patients at 40 clinical sites in the United States
- **Outcome Measures:**
  - Primary: Mean change from baseline to Week 4 in Mean Numeric Pain Rating Scale (NPRS) of pain in affected leg
  - Secondary: Mean change from baseline to Week 4 in Oswestry Disability Score Index (ODI)

Arm/Group Title	SP-102	Placebo
Arm/Group Description	SP-102 SP-102: injection	Placebo Placebo: injection

Period Title: **Overall Study**		
Started	202	199
Completed	193	192
Not Completed	9	7

Inclusion & Exclusion Criteria

- **Inclusion Criteria:** Ages 18-70, diagnosis of lumbar radiculopathy
- **Exclusion Criteria:** history of spine surgery, diagnosis of insulin dependent DM, BMI >40

Study Overview - Objectives

- Injection by healthcare professional with the possibility of a second injection as early as 1 month after first treatment
- **Objective:** measure the efficacy of a single injection of experimental SP-102 to provide relief of radicular symptoms and investigate the side effects of SP-102

Demographics

Age, Continuous
Mean (Standard Deviation) | Unit of measure: years

Number Analyzed	202 participants	199 participants	401 participants
	51.2 (9.83)	51.7 (10.36)	51.4 (10.09)

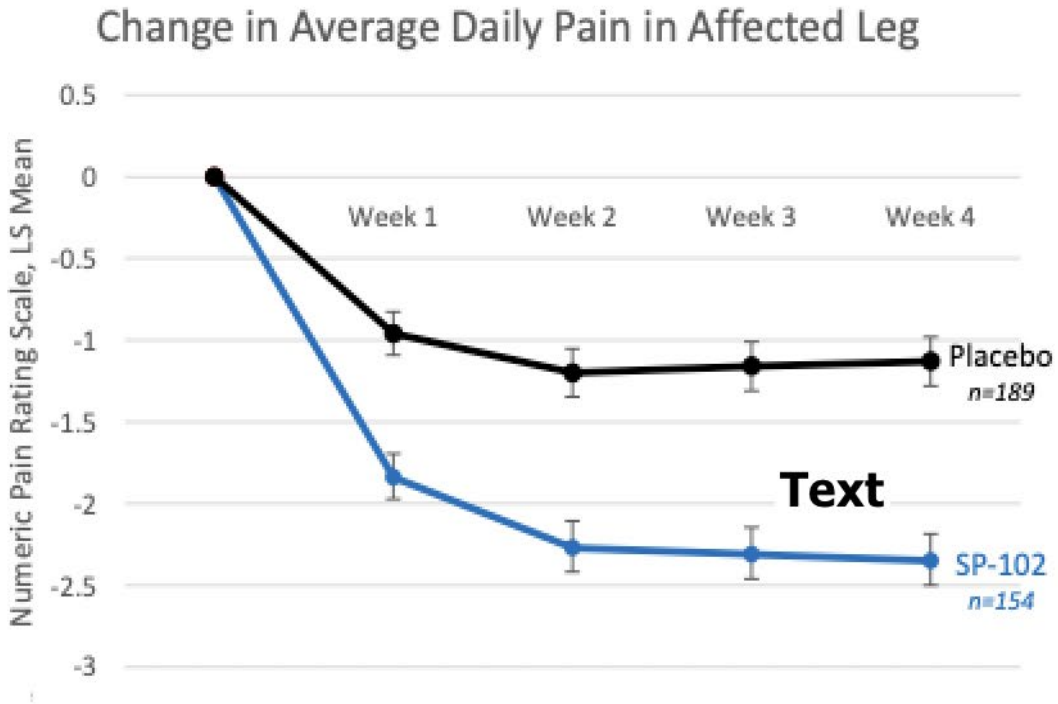
Sex: Female, Male
Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	202 participants	199 participants	401 participants
Female	116 57.4%	122 61.3%	238 59.4%
Male	86 42.6%	77 38.7%	163 40.6%

Race (NIH/OMB)
Measure Type: Count of Participants | Unit of measure: Participants

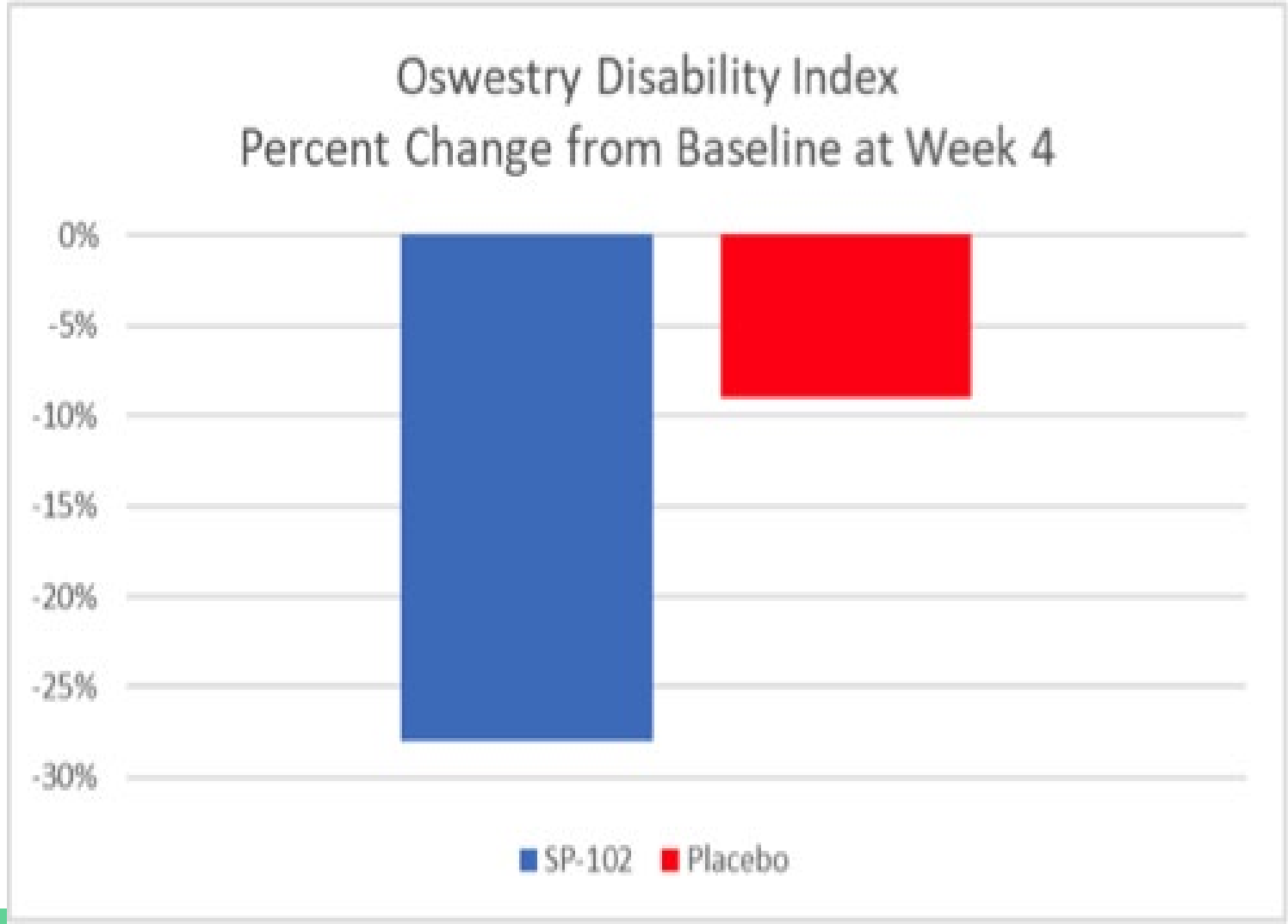
Number Analyzed	202 participants	199 participants	401 participants
American Indian or Alaska Native	0 0.0%	0 0.0%	0 0.0%
Asian	4 2.0%	3 1.5%	7 1.7%
Native Hawaiian or Other Pacific Islander	0 0.0%	0 0.0%	0 0.0%
Black or African American	37 18.3%	33 16.6%	70 17.5%
White	160 79.2%	162 81.4%	322 80.3%
More than one race	1 0.5%	1 0.5%	2 0.5%
Unknown or Not Reported	0 0.0%	0 0.0%	0 0.0%

Phase 3 SP-102 C.L.E.A.R Trial – Primary Endpoint



Comparison: SP-102 vs. Placebo	
Over 4 Weeks, LS Mean (SE)	-1.08 (0.17)
95% CI	-1.42, -0.75
p-value	<0.001***

The analysis used a restricted maximum likelihood (REML) based mixed model for repeated measures (MMRM) with fixed effects for treatment (SP-102 or placebo), week, site, Pain Catastrophizing Scale group (<30 or ≥30), baseline averaged daily leg pain score, and treatment-by-week interaction.


Oswestry Disability Index
Percent Change from Baseline at Week 4
0%
-5%
-10%
-15%
-20%
-25%
-30%
SP-102
Placebo

Adverse Events/Safety Profile

- No serious adverse events related to the drug or injection procedure
- No adverse events of special interest such as hematoma and infection at the injection site, or paraplegia were reported
- Established the safety of repeat injections, as patients who experienced moderate-to-severe radicular pain between 4 and 20 weeks were allowed to receive additional injection

The pharmacokinetics and pharmacodynamics of dexamethasone following epidural SP-102 or intravenous dexamethasone sodium phosphate injection in subjects with lumbosacral radicular pain

Shiyin Yee, Richard Robson, Elizabeth Stannard, Ritu Lal, Dmitri Lissin

PMID: 35818823 DOI: 10.5414/CP204221

Abstract

Objectives: To evaluate the pharmacokinetics, pharmacodynamics (PD), safety, and tolerability of epidural SP-102 (10 mg dexamethasone sodium phosphate injectable gel) compared to an intravenous injection of 10 mg dexamethasone sodium phosphate, USP (IV USP).

Materials and methods: Subjects with lumbosacral radiculopathy received a single dose of epidural SP-102, followed by a single dose of IV USP 4 weeks later. Dexamethasone plasma levels, cortisol levels, white blood cells (WBC), and blood glucose levels were assessed.

Results: Twelve subjects entered and completed the study. The mean total dexamethasone exposure (AUC_{last} and AUC_{inf}) following SP-102 by epidural injection was equivalent to the total exposure following IV USP. A lower mean plasma C_{max} (~ 50% lower) was observed following epidural administration compared to IV injection. PD parameters were similar between treatments. Adverse events (AEs) were mild, with no serious AEs or study discontinuations due to AEs.

Conclusion: In this small study, epidural SP-102 injection was well tolerated, was not associated with greater systemic dexamethasone exposure than IV USP, and both treatments had similar PD effects on cortisol suppression, blood glucose, and WBC levels.

Repeat Epidural Injections of SP-102 (Dexamethasone Sodium Phosphate Injectable Gel) in Subjects with Lumbosacral Radiculopathy

Richard Radnovich,[1] Jill Heinz,[1] Chris Ambrose,[2] Elizabeth Stannard,[2] and Dmitri Lissin[2]

Abstract Go to:

Purpose

SP-102 is a novel epidural steroid injection (ESI) formulation of 10 mg dexamethasone sodium phosphate in a viscous gel solution. Repeat dosing of ESIs is possible if required for pain relief, but with consideration of hypothalamic–pituitary–adrenal (HPA) axis suppression from prolonged systemic exposure. This phase I/II study investigated the effect of initial and repeat SP-102 injections on HPA suppression and analgesia.

Methods

Subjects with lumbosacral radiculopathy received an initial epidural SP-102 injection (T1) on day 1, followed by a repeat injection (T2) on ≥28 days later. To determine HPA suppression, area under the effect curve over 28 days and maximum change from baseline were calculated for cortisol, glucose levels, and white blood cell (WBC) count. Equivalent effect on HPA suppression of T1 relative to T2 was determined if the 90% CIs for ratios of these measures were within 80%–125%. The effect of repeat injections on leg and back pain was also assessed.

Results

Based on the responder analysis, all subjects had achieved a cortisol response by day 3 after initial injection and by day 2 after repeat injection. The repeat injection had similar effects on glucose levels and WBC count to the initial injection. Pain scores decreased after each injection and remained low for the 28-day follow-up, with some evidence of improved analgesic effect of the second dose compared with the first. There were no serious adverse events or discontinuations due to adverse events.

Conclusion

The lack of cumulative effect and rapid resolution of HPA suppression following repeated SP-102 dosing suggests that consideration of HPA pharmacodynamics is not clinically relevant when making decisions regarding repeat dosing. SP-102 ESIs provided prolonged pain relief, with preliminary evidence of greater efficacy after repeat injection. A phase III trial is ongoing.