Early Response of SI-6603 (Condoliase) for Radicular Leg Pain Associated with Lumbar Disc Herniation

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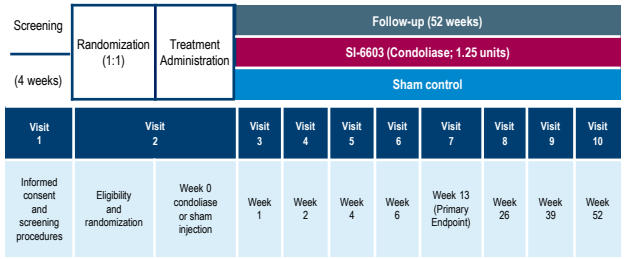
BACKGROUND

- Lumbar disc herniation (LDH) is associated with substantial clinical and economic burden due to accompanying symptoms, including pain[1]
- Prolonged duration of LDH symptoms (ie, >6 months) is associated with worse outcomes[2,3]
- SI-6603 (condoliase) is a novel chemonucleolytic enzyme with high substrate specificity for degrading glycosaminoglycans (primarily chondroitin sulfate) in the nucleus pulposus[4,5]
- Condoliase was approved in Japan in 2018 as a single intradiscal injection for the treatment of radicular leg pain associated with LDH[6,7]
- This analysis of a United States phase 3 clinical trial (NCT03607838) evaluates the early treatment response (ie, ≤6 weeks) to condoliase in participants with LDH associated with radicular leg pain

Figure 1. Study Design



STUDY DESIGN AND PARTICIPANTS

- Inclusion criteria: Adults 30 to 70 years of age with contained posterolateral LDH, radicular leg pain, positive straight leg raise (SLR) test (≤70° on the ipsilateral leg), and >6 weeks of conservative treatment
- Primary endpoint: Change from baseline (CFB) to Week 13 in worst leg pain (past 24 hours averaged over previous 7 days) as assessed by 100-mm visual analogue scale (VAS)
- Supportive endpoints (exploratory in nature): CFB in worst leg pain, percentage of participants with negative SLR test, and 50% responder rates (participants with ≥50% improvement from baseline) for worst leg pain and Oswestry Disability Index (ODI)
- CFB in worst leg pain at all timepoints was assessed using a mixed model for repeated measures analysis
- The percentage of participants with negative SLR test and 50% responders for worst leg pain and ODI were compared between treatment groups with a difference in proportions Z test

KEY TAKEAWAYS

1. **Condoliase met its primary endpoint of significantly improving worst leg pain at Week 13 in this US phase 3 clinical trial**
2. **Condoliase was associated with rapid improvements (≤6 weeks post treatment) in radicular leg pain**
3. **The early treatment effect of condoliase emphasizes its potential to offer a treatment option for patients with LDH**
4. **Condoliase was safe and well tolerated, with no treatment-related serious adverse events**

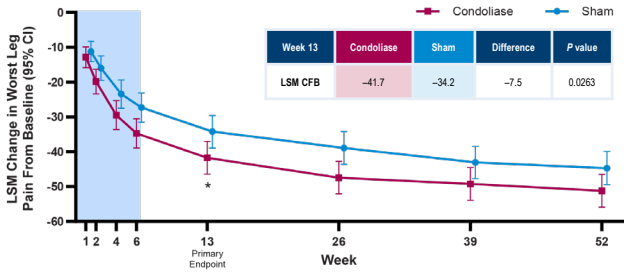
RESULTS

Table 1. Baseline Participant Characteristics

	Condoliase (n=169)	Sham (n=172)
Age, mean (SD), years	46.8 (9.4)	45.9 (9.8)
Female sex, n (%)	74 (43.8)	83 (48.3)
Race, n (%)		
White	137 (81.1)	142 (82.6)
Black/African American	18 (10.7)	14 (8.1)
Asian	6 (3.6)	9 (5.2)
Other[a]	8 (4.7)	7 (4.1)
Screening BMI, mean (SD), kg/m²	29.0 (4.9)	28.4 (4.9)
Current/past smoker, n (%)	63 (37.3)	69 (40.1)
Heavy labor, n (%)	39 (23.1)	49 (28.5)
Worst leg pain, mean (SD), mm	72.0 (9.6)	71.8 (9.8)
ODI score, mean (SD)	48.2 (11.8)	49.1 (11.9)
Herniation site, n (%)		
L4-L5	70 (41.4)	71 (41.3)
L5-S1	99 (58.6)	101 (58.7)

Baseline participant characteristics were similar across treatment groups

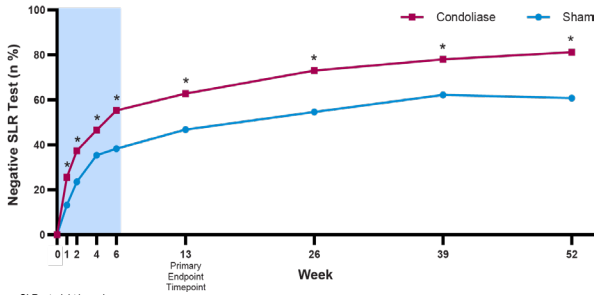
Figure 2. LSM CFB in Average Worst Leg Pain



CFB, change from baseline; CI, confidence interval; LSM, least squares mean.
*Denotes statistical significance, $P<0.05$.

Beginning at Week 1, the condoliase group showed numerically greater improvements in worst leg pain vs sham

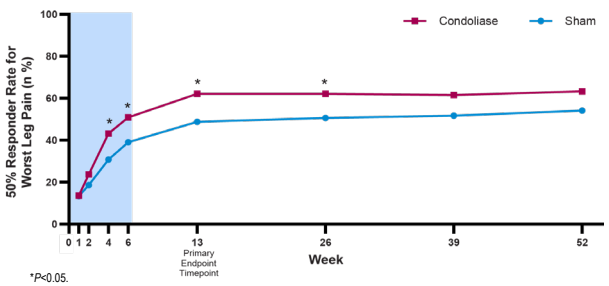
Figure 3. Negative SLR Test



SLR, straight leg raise.
*$P<0.05$.

Beginning at Week 1, the condoliase group had a higher percentage of participants (vs sham) with a negative SLR test

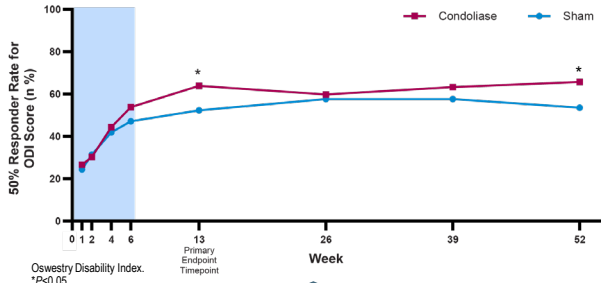
Figure 4. 50% Responders – Worst Leg Pain



*$P<0.05$.

The 50% responder rate for worst leg pain favored condoliase beginning at Week 4 compared with sham

Figure 5. 50% Responders – ODI Score



Oswestry Disability Index.
*$P<0.05$.

Notable differences in 50% responder rates for ODI favoring condoliase occurred at Week 13

Table 2. Summary of Adverse Events

n (%)	Condoliase (n=167)	Sham (n=174)
Any TEAE	120 (71.9)	105 (60.3)
Mild	76 (45.5)	65 (37.4)
Moderate	31 (18.6)	29 (16.7)
Severe	13 (7.8)	11 (6.3)
Any treatment-related TEAE	47 (28.1)	18 (10.3)
Any SAE	7 (4.2)	6 (3.4)
Treatment-related SAE	0	0
AEs leading to study discontinuation	2 (1.2)	4 (2.3)
TEAEs in ≥5% of participants[a]		
Abnormal spinal MRI	47 (28.1)	16 (9.2)
Back pain	32 (19.2)	22 (12.6)
Pain in extremity	18 (10.8)	13 (7.5)
Abnormal spinal X-ray	13 (7.8)	3 (1.7)
COVID-19	11 (6.6)	17 (9.8)
C-reactive protein increased	10 (6.0)	6 (3.4)
Sciatica	6 (3.6)	9 (5.2)
Any AESI	87 (52.1)	55 (31.6)

[a]By preferred term, classified according to MedDRA version 24.0.
AE, adverse event; AESI, adverse event of special interest; COVID-19, Coronavirus disease 2019; MedDRA, Medical Dictionary for Regulatory Activities; MRI, magnetic resonance imaging; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

No adverse events (AEs) leading to study discontinuation or serious AEs were considered treatment-related

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