

Cryoneurolysis for Knee Osteoarthritis in a Real-world Registry: Pain and Functional Outcomes Over 12 Months

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OBJECTIVE

To evaluate real-world pain and functional outcomes from the Innovations in Genicular Outcomes Registry (IGOR) following cryoneurolysis therapy for knee osteoarthritis (OA)

CONCLUSIONS

1 Treatment with cryoneurolysis in patients with knee OA was associated with long-term reductions in pain and improved function in a real-world setting over 12 months

- Cryoneurolysis was relatively more effective compared with conventional intra-articular (IA) agents, most of which typically provide pain relief and functional improvement for 4-6 months; patients receiving IA corticosteroids or nonsteroidal anti-inflammatory drugs required a new treatment at 6 months

2 These data support the use of cryoneurolysis for long-term pain management in patients with knee OA

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INTRODUCTION

Cryoneurolysis is a denervation-based therapy that uses low temperatures (-20°C to -100°C) to induce Wallerian degeneration and reversible disruption of nerve function to reduce pain for extended periods¹

- Cryoneurolysis uses a coolant (eg, liquid nitrous oxide) contained within a device and needle tips to create a precise cold zone at target nerve sites²

- This approach causes peripheral nerve degeneration distal to the treatment that preserves the epineurium, perineurium, and endoneurium, thereby allowing for nerve regrowth^{2,3}

• Because cryoneurolysis is a novel treatment for pain in knee OA, additional evidence is needed to further characterize its safety and efficacy in a real-world setting¹

• IGOR is a prospective, observational registry that comprises a standardized collection of real-world knee OA data, including clinical, patient-reported, reimbursement, and healthcare resource utilization outcomes,⁴ enhancing the way in which clinical decision-making is performed by treating physicians and their patients

RESULTS

PATIENT CHARACTERISTICS AND DEMOGRAPHICS AT SCREENING

• Of 129 patients who received cryoneurolysis, 75 received Cryo-Deep/Both (Deep: n=6; Both: n=69) and 54 received Cryo-Superficial; all patients were evaluated for 12 months following treatment (Table 1)

• Most patients who received cryoneurolysis were female (79%) and white (74%; Table 1)

• The mean (standard deviation [SD]) follow-up time since knee OA treatment was 258 (193) days for those treated with Cryo-Deep/Both and 158 (154) days for those treated with Cryo-Superficial

• Mean (SD) pain intensity, as measured on the BPI-Pain scale, was moderate for both treatments (5.4 [2.1] for Cryo-Deep/Both and 6.4 [2.4] for Cryo-Superficial)

• Mean (SD) functional outcome at screening, as measured on the KOOS, JR scale, was poor for both treatment groups (44.1 [14.4] for Cryo-Deep/Both and 32.2 [14.2] for Cryo-Superficial)

Table 1. Key Patient Demographics and Baseline Characteristics

	Cryo-Deep/Both (n=75)*	Cryo-Superficial (n=54)
Follow-up time following treatment, mean (SD), d	258 (193)	158 (154)
Age, mean (SD), y	65.7 (9.5)	63.5 (11.6)
Female, n (%)	63 (84)	39 (72)
Body mass index, mean (SD), kg/m²	35.6 (10.1)	34.0 (8.2)
K-L grade, n (%)		
1 (doubtful)	5 (7)	1 (2)
2 (mild)	13 (18)	3 (6)
3 (moderate)	35 (47)	7 (14)
4 (severe)	21 (28)	40 (78)
BPI-Pain score, mean (SD)	5.4 (2.1)	6.4 (2.4)
KOOS, JR, mean (SD)	44.1 (14.4)	36.4 (19.5)
PCS, mean (SD)	23.9 (13.2)	32.2 (14.2)

*Deep: n=6; Both: n=69. BPI-Pain, Brief Pain Inventory pain scale; Cryo-Deep/Both, cryoneurolysis of the deep genicular and superficial genicular nerves; Cryo-Superficial, cryoneurolysis of the superficial nerves; K-L, Kellgren-Lawrence; KOOS, JR, Knee Injury and Osteoarthritis Outcome Score for Joint Replacement; PCS, pain catastrophizing scale; SD, standard deviation.

METHODS

STUDY DESIGN

• In this prospective, observational, registry-based real-world study, 2 cryoneurolysis approaches were evaluated in adult patients with primary knee OA

- Deep genicular and superficial genicular nerve block together (Cryo-Deep/Both)
- Superficial nerve block (Cryo-Superficial)

• Data on pain and functional outcomes were collected from IGOR for up to 12 months of follow-up after cryoneurolysis treatment

STUDY OUTCOMES AND STATISTICAL ANALYSIS

• The main outcomes of the study included

- Time to next knee OA treatment, including but not limited to multiple IA treatments (ie, corticosteroids, hyaluronic acid, nonsteroidal anti-inflammatory drugs, platelet-rich plasma, triamcinolone acetonide extended-release injection), cryoneurolysis, and knee replacement

- Pain severity from the Brief Pain Inventory pain scale (BPI-Pain)

• BPI-Pain severity scores range from 0 to <4 ("mild pain"), 4 to <7 ("moderate pain"), and 7 to 10 ("severe pain")

- Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS, JR) functional outcomes

• Scores range from 0 to 70; lower scores reflect worse function

• Changes in BPI-Pain and functional KOOS, JR scores from screening were assessed weekly over the first 6 weeks, monthly from month 2 through month 6, and then every 3 months thereafter (ie, month 9 and month 12)

• The least squares mean (LSM) for BPI-Pain scores and KOOS, JR functional outcomes scores were estimated over time by a linear mixed-effects model; estimated changes were adjusted for age, sex, base score, Kellgren-Lawrence (K-L) grade, baseline pain catastrophizing scale, treatment time, and follow-up opioid use

TIME TO NEXT TREATMENT

• Cryo-Deep/Both resulted in improved survival: 46% of patients receiving Cryo-Deep/Both required repeat treatment by 385 days (12.8 months) and 49% of patients receiving Cryo-Superficial required repeat treatments within 184 days (6 months)

• In contrast, approximately 70% of participants receiving IA injections switched to the next treatment after 6 months (Figure 1B)

- Patients receiving platelet-rich plasma and hyaluronic acid IA injections did not switch to the next treatment; this is likely because they experienced less pain before treatment

PAIN OUTCOMES

• Patients treated with cryoneurolysis experienced moderate pain over 12 months (Figure 2A)

- Pain severity was lower than screening at the first follow-up visit (week 1) for both cryoneurolysis treatments, with LSM BPI-Pain scores ≤4.5 (approximately in the mild severity range; Figure 2A)

- By month 12, LSM BPI-Pain scores were 4.7 and 5.6 for Cryo-Deep/Both and Cryo-Superficial, respectively

• The magnitude of the reduction in pain severity was statistically significant starting at week 1 for patients receiving Cryo-Deep/Both, which was maintained through the 12-month follow-up (P<0.01); in contrast, the Cryo-Superficial group demonstrated early but not statistically significant reduction from baseline pain through 12 months (Figure 2B)

• Patients treated with cryoneurolysis experienced better function over 12 months (Figure 3A)

- LSM KOOS, JR functional scores were ~1.5-fold higher than at the first follow-up visit (week 1) versus screening for both cryoneurolysis treatments (56.6 vs 39.0 for Cryo-Deep/Both and 59.1 vs 37.8 for Cryo-Superficial; Figure 3A)

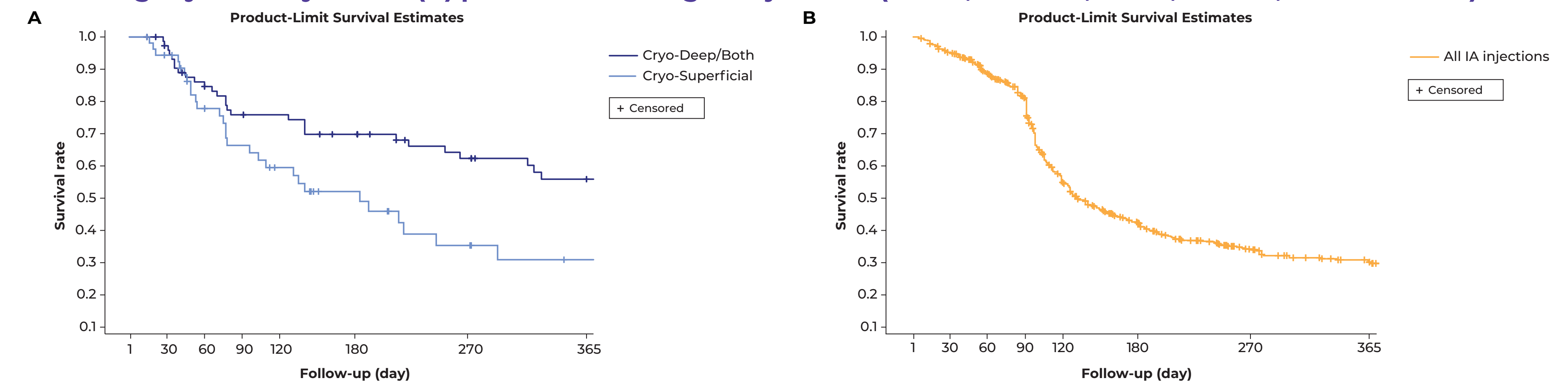
- By month 12, LSM KOOS, JR functional scores were 53.4 and 41.5 for Cryo-Deep/Both and Cryo-Superficial, respectively

- There was no statistically significant difference between the 2 Cryo-Deep/Both and Cryo-Superficial groups with respect to the trajectory of functional recovery (P=0.139)

• The magnitude of functional improvement from screening, as assessed by KOOS, JR was significant starting at week 1 for patients receiving either cryoneurolysis treatment (P<0.01; Figure 3B)

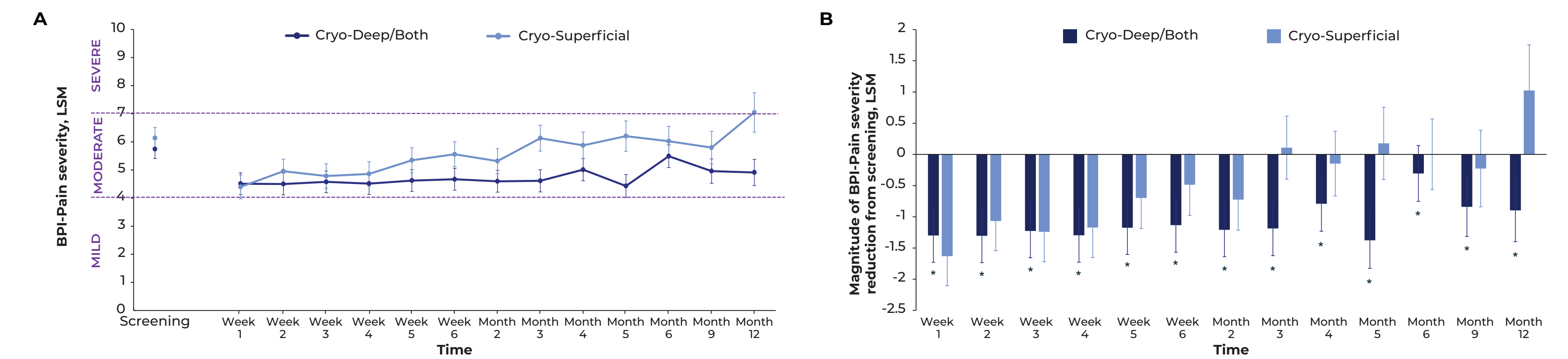
- Significant improvements in function were maintained through the 12-month follow-up for both the Cryo-Deep/Both and Cryo-Superficial groups (P<0.01; Figure 3B)

Figure 1. Time to next treatment according to enrollment treatment. Kaplan-Meier survival analyses of (A) patients receiving cryoneurolysis and (B) patients receiving IA injections (IA-HA, IA-TAER, IA-CS, IA-PRP, and IA-NSAID).



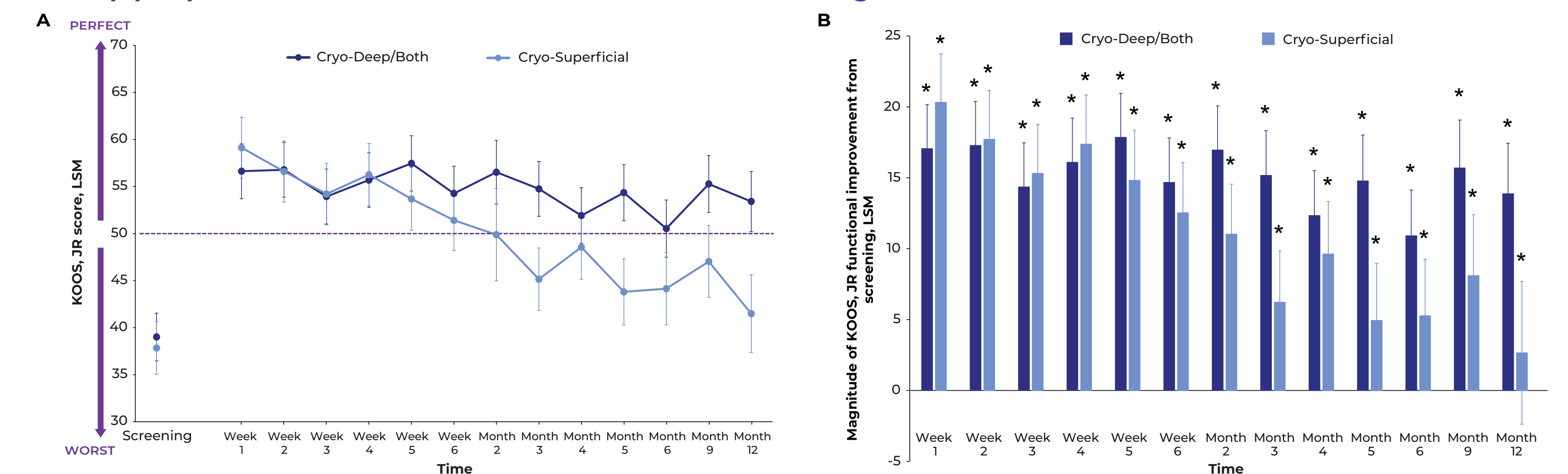
Cryo-Deep/Both, cryoneurolysis of the deep genicular and superficial genicular nerves; Cryo-Superficial, cryoneurolysis of the superficial nerves; CS, corticosteroid; HA, hyaluronic acid; IA, intra-articular; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; TAER, triamcinolone acetonide extended-release.

Figure 2. LSM BPI-Pain severity over time following cryoneurolysis. (A) Pain severity over time. (B) Reductions in pain severity from screening.



Error bars are the standard error. *P<0.01. BPI-Pain, Brief Pain Inventory pain scale; Cryo-Deep/Both, cryoneurolysis of the deep genicular and superficial genicular nerves; Cryo-Superficial, cryoneurolysis of the superficial nerves; LSM, least squares mean.

Figure 3. LSM KOOS, JR functional outcomes over time following cryoneurolysis. (A) Functional outcomes over time. (B) Improvements in functional outcomes from screening.



Error bars are the standard error. *P<0.01. Cryo-Deep/Both, cryoneurolysis of the deep genicular and superficial genicular nerves; Cryo-Superficial, cryoneurolysis of the superficial nerves; KOOS, JR, Knee Injury and Osteoarthritis Outcome Score for Joint Replacement; LSM, least squares mean.