Innovations in Genicular Outcomes Registry (iGOR): Osteoarthritis of the Knee (OAK) Pain Outcomes

Andrew I. Spitzer,[1] Vinod Dasa,[2] Adam Rivadeneyra,[3] David Rogenmoser,[4] Joshua Urban,[5] Michael A. Mont,[6] Andrew Concoff,[7] Jennifer H. Lin,[8] William Mihalko[9]

[1]Cedars Sinai Medical Center, Los Angeles, CA; [2]Louisiana State University Health Services Center, New Orleans, LA; [3]Orthopaedic Specialty Institute, Orange, CA; [4]Mid State Orthopaedic & Sports Medicine Center, Alexandria, LA; [5]OrthoNebraska, Omaha, NE; [6]Sinai Hospital of Baltimore, Baltimore, MD; [7]Exagen Inc., Vista, CA; [8]Pacira BioSciences, Inc., Tampa, FL; [9]University of Tennessee Health Science Center, Campbell Clinic Orthopaedics, Memphis, TN

FINANCIAL DISCLOSURES

AS has given paid presentations and received research fees from DePuy and Pacira BioSciences, Inc., and received consultancy fees from DePuy, Flexion Therapeutics, Pacira BioSciences, Inc., and TraumaCad.

VD has given paid presentations for BioVentus, Pacira BioSciences, Inc., and Sanaral; has received consulting fees from Bioventus, Cymedica, Ferring Pharmaceuticals, Medi Post, Pacira BioSciences, Inc., Sanofi-Aventis, and Vertex Pharmaceuticals; has stock in Cymedica, Doc Social, Goldfinch Consulting, Grand Care, MEND, mymedicalimages.com, and SIGHT Medical; receives research funding from Cartiheal and Pacira BioSciences, Inc.; and serves on the editorial board of the *Journal of Orthopedic Experience and Innovation*.

AR has given paid presentations and received consultancy fees from Pacira Biosciences, Inc.

DR has received consultancy fees from Pacira BioSciences, Inc.

JU has given paid presentations and received consultancy fees from Pacira BioSciences, Inc., has received research support from Pacira BioSciences, Inc., SpineBioPharma, and Vertex; and has stock in Pacira BioSciences, Inc.

MM has received consulting fees from 3M, CERAS Health, Exactech, Johnson & Johnson, Mirror-AR, NXSCI, Pacira BioSciences, Inc., Peerwell, Smith & Nephew, Stryker, and US Medical Innovations; research funding from the National Institutes of Health; royalties from Stryker; serves as a board member for the Hip Society and the Knee Society; and is an Editor for the *Journal of Arthroplasty*, the *Journal of Knee Surgery*, *Surgical Technology International*, and *Orthopaedics*.

AC is an employee of Exagen and owns stock and has received consultancy fees from Pacira BioSciences, Inc., and United Rheumatology.

JHL is an employee of Pacira BioSciences, Inc., and own stock in this company.

WM has given paid presentations and received consulting fees from Aesculap/B. Braun. and Pacira Biosciences, Inc.; owns stock in Medtronic; received research support from the American Association of Hip and Knee Surgeons, the Food and Drug Administration, and Medacta; received other financial support and royalties from Saunders/Mosby-Elsevier; received royalties from Aesculap/B. Braun; serves on the editorial board for the *Journal of Arthroplasty*, the *Journal of Long Term Effects of Medical Implants*, the *Journal of Orthopaedic Research*, and *Orthopedic Clinics of North America*; and serves as a board member for the American Association of Hip and Knee Surgeons, the American Academy of Orthopedic Surgeons, the American Society for Testing and Materials, the Campbell Foundation, the Hip Society, the Knee Society, the International Society for Technology in Arthroplasty, and the Orthopaedic Research Society.

INTRODUCTION

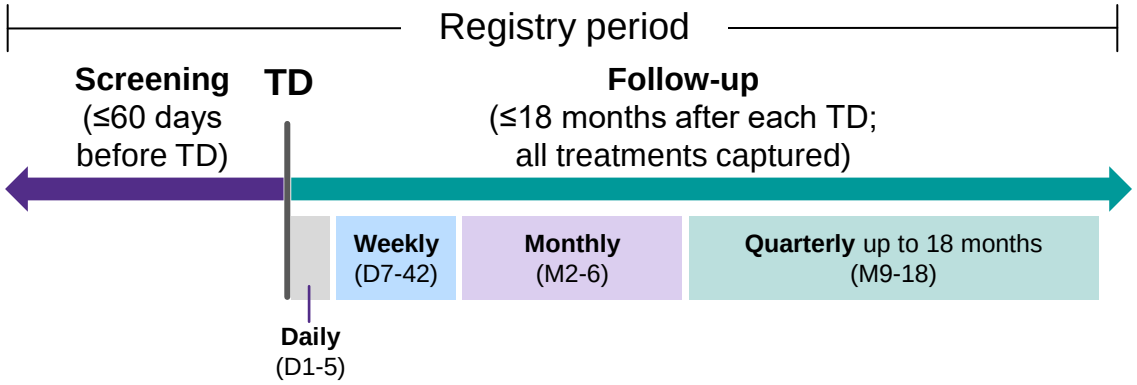
- Treatment of OAK, focused on reducing pain and improving function,[1] is often long term and involves multiple treatment modalities given chronicity of disease and individual patient considerations over time (eg, comorbidities, goals)[2]
  - Although innovative nonsurgical OAK treatments (eg, extended-release injectable corticosteroid treatment, cryo nerve block) have been investigated in clinical studies,[3-5] data are needed to further characterize these treatment options in real-world settings
  - Additionally, clinical trial design restricts populations based on inclusion criteria and generally lacks longer term follow-up that may help inform treatment decisions
  - **The iGOR is a prospective, observational, longitudinal, multi-center registry designed to compare the effectiveness of several health outcomes among interventions chosen to manage symptomatic OAK through shared decision-making between physicians and patients**
  - The inclusive and comprehensive design of iGOR enables an assessment of outcomes of multiple OAK treatments across dynamic treatment paradigms, reflecting real-world practice

Objective: To report comparative pain and function outcomes for multiple nonsurgical treatments for OAK in this early analysis of an ongoing iGOR prospective study

iGOR, Innovations in Genicular Outcomes Registry; OAK, osteoarthritis of the knee; TKA, total knee arthroplasty. 1. The American Academy of Orthopaedic Surgeons. Management of osteoarthritis of the knee (non-arthroplasty): evidence-based clinical practice guideline. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2021; 2. Nalamachu SR et al. *J Pain Res*. 2020;13:3415-3425; 3. Conaghan PG et al. *J Bone Joint Surg Am*. 2018;100(8):666-677; 4. Langworthy MJ et al. *Adv Ther*. 2019;36(6):1398-1411; 5. Radnovich R et al. *Osteoarthritis Cartilage*. 2017;25(8):1247-1256.

METHODS: Registry and Study Design

- The iGOR (NCT05495334) is an observational registry, with all treatment decisions made by patients and their providers in a shared decision-making manner
- Participants enrolled in iGOR complete electronic instruments before (baseline) and after treatment to assess pain, function, sleep disturbance, quality of life, and satisfaction over 18 months



Current Analysis

Eligibility:
- ≥1 month of follow-up
- Unilateral OAK
- Moderate-to-severe pain before treatment baseline (≥4 on the BPI-sf; scale ranging from 0 [no pain] to 10 [worst])

Study Location/Period: 6 US clinical sites from September 24, 2021, to December 30, 2022

Treatments (1 of 5):
- IA-hyaluronic acid (IA-HA)
- IA-ketorolac (IA-NSAID)
- IA-conventional corticosteroids (IA-CS)
- IA-triamcinolone acetonide extended-release (IA-TA-ER)
- Genicular-nerve cryoneurolysis (Cryo)

Outcome	Measure*
Pain severity	BPI-sf
Function	KOOS-JR†

*Multivariable mixed-effects modeling was conducted for outcome comparisons between treatments with adjustment for age, sex, study site, KL grade, baseline pain severity or function scores, pain catastrophizing, and follow-up analgesic use. †Interval score with a scale ranging from 0 (worst) to 100 (perfect); assessed at Weeks 1 through 6, then at 2 and 3 months. BPI-sf, Brief Pain Inventory short form; IA, intraarticular; iGOR, Innovations in Genicular Outcomes Registry; KL, Kellgren-Lawrence; KOOS-JR, Knee Injury and Osteoarthritis Outcome Score for Joint Replacement; OAK, osteoarthritis of the knee; TD, treatment day; TKA, total knee arthroplasty.

RESULTS: Patient Demographics and Baseline Characteristics

Of 178 total patients who were enrolled and received OAK pain treatment, the mean (SD) age was 61 (10) years, 75% of patients were female, and 24% were Medicaid beneficiaries

- Most baseline variables were similar across treatment groups besides sex, BMI, and target knee treatment in the past year
- The mean BMI was >30 kg/m^2 across the 5 treatment cohorts
- Overall, 68% of patients had a KL grade of 3 (moderate) or 4 (severe)

	IA-HA (n=21)	IA-NSAID (n=19)	IA-CS (n=75)	IA-TA-ER (n=15)	Cryo (n=48)	Total (N=178)	*P* value*
Age, mean (SD), y	63 (11)	59 (10)	60 (9)	63 (11)	63 (10)	61 (10)	0.14
Sex, n (%)							0.03
Female	16 (76)	16 (84)	47 (63)	12 (80)	42 (88)	133 (75)	
Race, n (%)							0.39
Asian	0	0	1 (1)	1 (7)	0	2 (1)	
Black or African American	5 (24)	10 (53)	25 (33)	3 (20)	13 (27)	56 (31)	
Native Hawaiian or other Pacific Islander	0	0	1 (1)	0	0	1 (1)	
Unknown	1 (5)	0	7 (9)	1 (7)	1 (2)	10 (6)	
White	15 (71)	9 (47)	41 (55)	10 (67)	34 (71)	109 (61)	
BMI, mean (SD), kg/m^2	32 (6)	41 (11)	34 (8)	36 (10)	36 (8)	35 (9)	0.02
Insurance type, n (%)							<0.001
Commercial/Private	9 (43)	4 (21)	48 (64)	4 (27)	21 (44)	86 (48)	
Medicaid	5 (24)	9 (47)	13 (17)	2 (13)	13 (27)	42 (24)	
Medicare	9 (43)	7 (37)	19 (25)	9 (60)	30 (63)	74 (42)	
Other	0	0	0	0	2 (4)	2 (1)	
Target knee left, n (%)	4 (19)	10 (53)	31 (41)	8 (53)	17 (35)	70 (39)	0.15
KL grade, n (%)							0.18
1 (doubtful)	0	0	5 (7)	0	3 (6)	8 (4)	
2 (minimal)	7 (33)	5 (26)	21 (28)	3 (20)	11 (23)	47 (26)	
3 (moderate)	6 (29)	3 (16)	31 (41)	4 (27)	13 (27)	57 (32)	
4 (severe)	8 (38)	11 (58)	18 (24)	8 (53)	19 (40)	64 (36)	
Target knee treatment in the past year, n (%)							<0.001
Cryo or RFA	0	2 (11)	0	1 (7)	6 (13)	9 (5)	
HA	7 (33)	5 (26)	4 (5)	2 (13)	0	18 (10)	
IA-Steroid	8 (38)	5 (26)	13 (17)	9 (60)	21 (44)	56 (31)	
Surgery	7 (33)	5 (26)	12 (16)	7 (47)	5 (10)	36 (20)	

*Categorical variables were tested by the chi-square method and continuous variables were tested by the Kruskal-Wallis test.

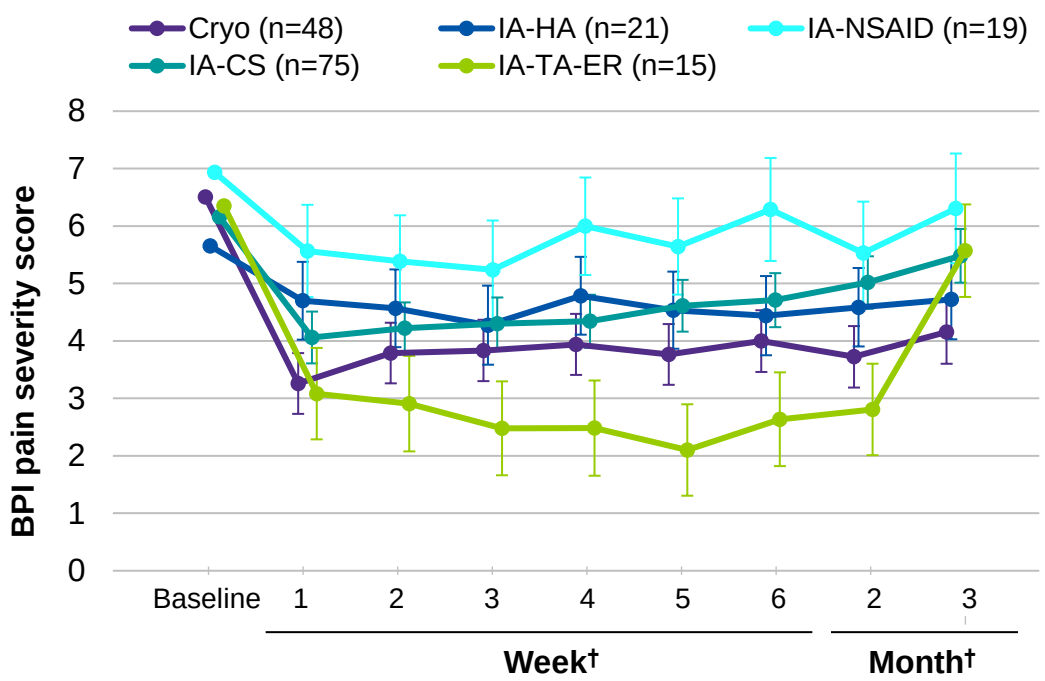
BMI, body mass index; Cryo, cryoneurolysis; KL, Kellgren-Lawrence; IA-CS, intraarticular conventional corticosteroids; IA-HA, intraarticular hyaluronic acid; IA-NSAID, intraarticular ketorolac; IA-TA-ER, intraarticular triamcinolone acetonide extended-release; OAK, osteoarthritis of the knee; SD, standard deviation.

RESULTS: Pain Severity Outcomes

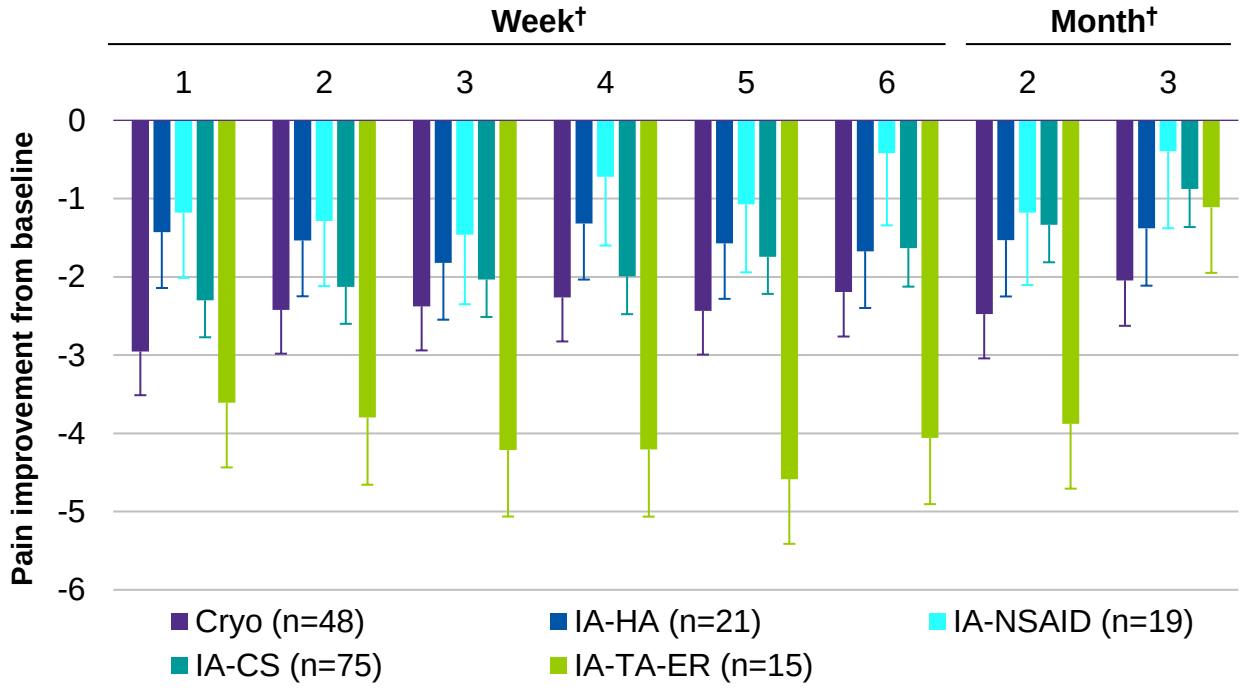
During the 3 months of follow-up after treatment, pain severity was reduced from baseline for all treatments (left)

Reduction of pain from baseline was significant for most treatments (except IA-NSAID), with IA-TA-ER associated with the greatest reduction from baseline* (right)

Post-Treatment BPI Pain Severity Scores During 3 Months of Follow-up



Reduction of Post-Treatment BPI Pain Severity Scores (From Baseline) During 3 Months of Follow-up

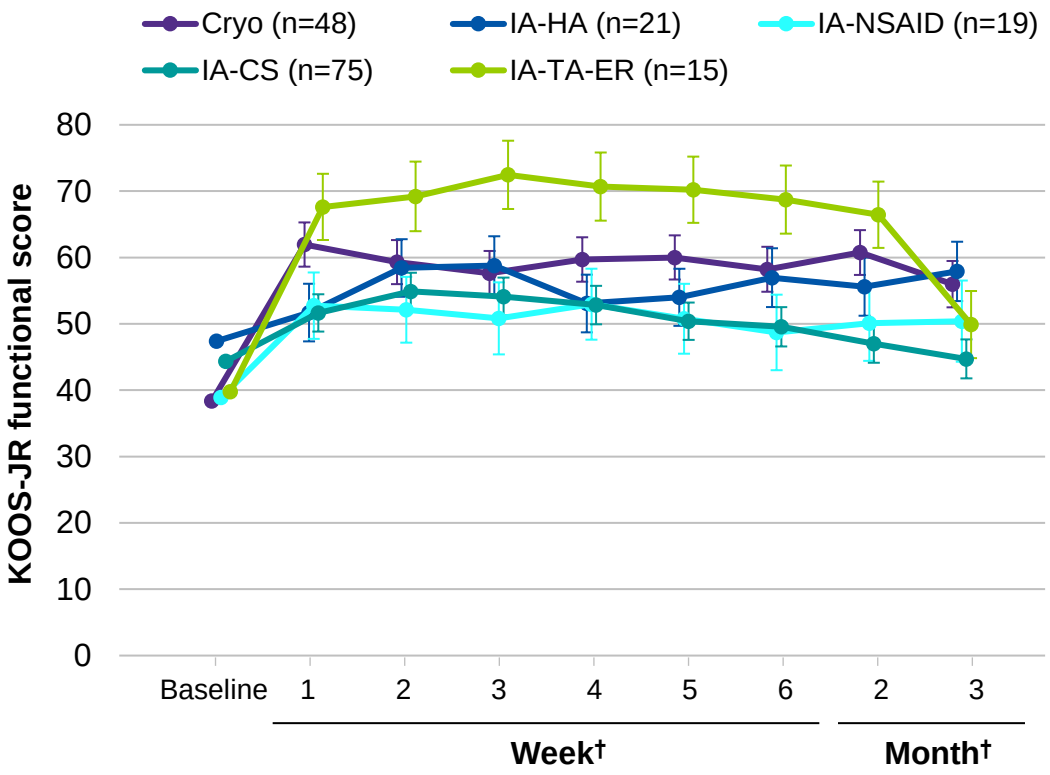


*Similar results were obtained after additional analyses incorporating adjustments for insurance type and body mass index. †Adjusted pain score after treatment. BPI, Brief Pain Inventory; Cryo, cryoneurolysis; IA-CS, intraarticular conventional corticosteroids; IA-HA, intraarticular hyaluronic acid; IA-NSAID, intraarticular ketorolac; IA-TA-ER, intraarticular triamcinolone acetonide extended-release. Error bars are the standard error.

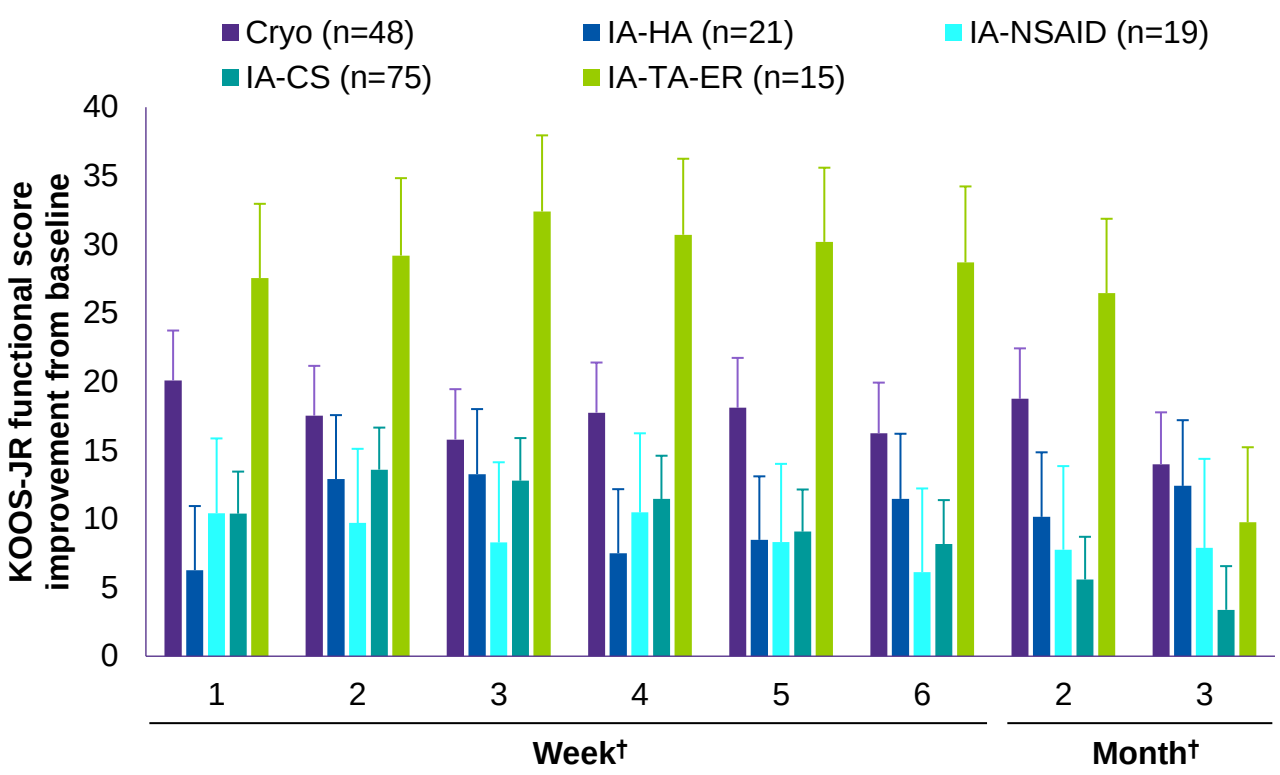
RESULTS: Functional Outcomes

Over the 3-month follow-up period, numerical improvements from baseline in KOOS-JR scores were observed for all treatments,* with IA-TA-ER injection associated with greatest functional improvement compared with all other IA injections

Post-Treatment KOOS-JR Functional Scores During 3 Months of Follow-up



Improvement of Post-Treatment KOOS-JR Functional Scores (From Baseline) During 3 Months of Follow-up

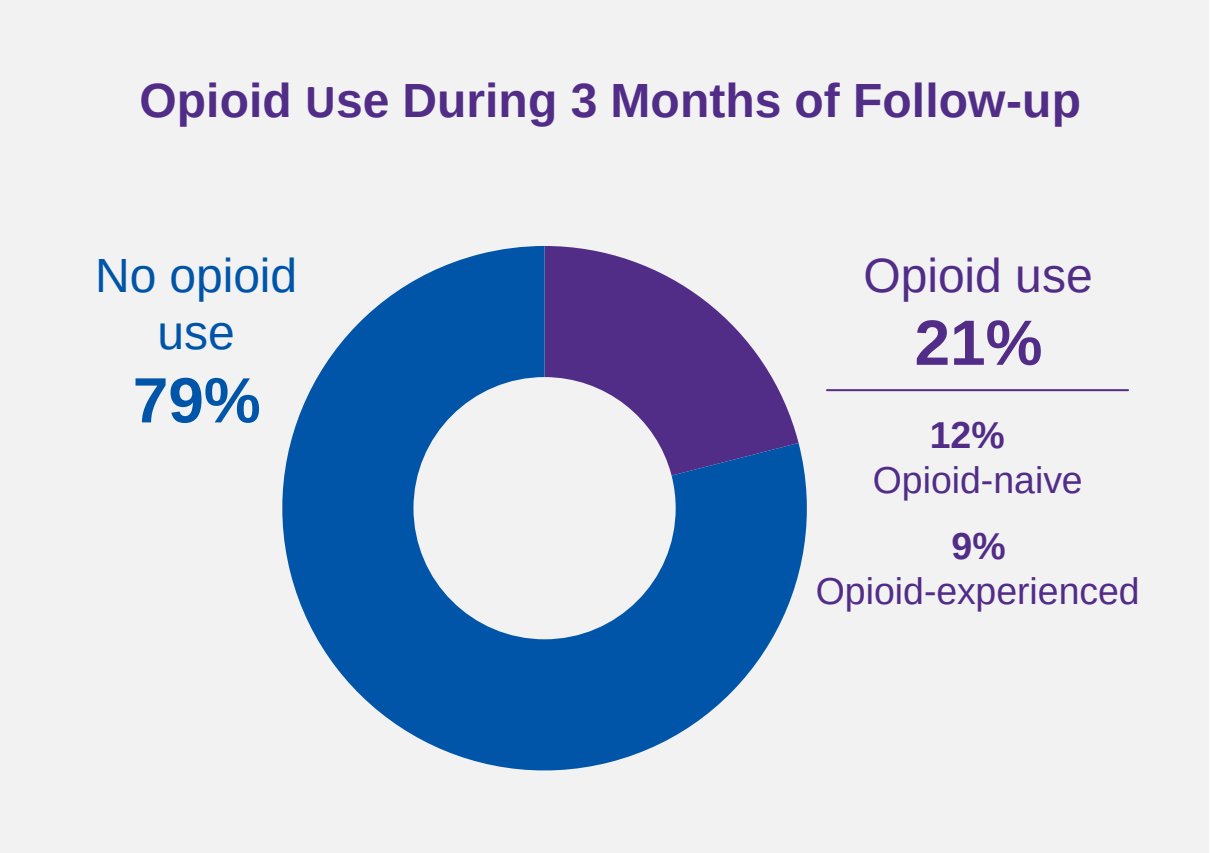


*Similar results were obtained after additional analyses incorporating adjustments for insurance type and body mass index. †Adjusted score after treatment. Cryo, cryoneurolysis; IA-CS, intraarticular conventional corticosteroids; IA-HA, intraarticular hyaluronic acid; IA-NSAID, intraarticular ketorolac; IA-TA-ER, intraarticular triamcinolone acetonide extended-release; KOOS-JR, Knee Injury and Osteoarthritis Outcome Score for Joint Replacement. Error bars are the standard error.

RESULTS: Opioid Use Outcomes

In this iGOR analysis including patients who received nonsurgical treatments for OAK, 38 patients of 178 total patients (21%) reported using opioids during the follow-up period

- 22 of 178 total patients (12%) who used opioids during follow-up had not taken opioids before treatment (opioid naive)



iGOR, Innovations in Genicular Outcomes Registry; OAK, osteoarthritis of the knee.

CONCLUSIONS

1. Early results from the iGOR, a unique, first-of-its-kind, inclusive, and comprehensive registry, exhibited the feasibility of using a registry to obtain real-world data for the comparative effectiveness of OAK treatments

2. In the current analyses, numerical improvements in pain and function were observed for 5 nonsurgical OAK treatments

   - The IA-TA-ER cohort showed the highest magnitude of improvements over other treatments, while Cryo was associated with greater improvement than IA-NSAID in pain and IA-CS in function

   - While these findings may be impacted by residual confounding, plausible confounders including age, sex, BMI, KL grade, baseline pain catastrophizing scale score, and analgesic medication were controlled in the multivariable regression model

3. These preliminary findings reflect results of a relatively small sample; as registry enrollment continues, longer term data from larger samples will improve understanding of the real-world impact of OAK treatments and inform future analyses

BMI, body mass index; Cryo, cryoneurolysis; IA-CS, intraarticular conventional corticosteroids; iGOR, Innovations in Genicular Outcomes Registry; KL, Kellgren-Lawrence, OAK, osteoarthritis of the knee; IA-NSAID, intraarticular ketorolac; IA-TA-ER, intraarticular triamcinolone acetonide extended-release.