2103

PCRX-201 High-Capacity Adenovirus Serotype 5 Gene Therapy Demonstrates Sustained Clinical Efficacy and Safety in Patients With Knee Osteoarthritis

Stanley Cohen,[1] Philip G. Conaghan,[2] Marc C. Hochberg,[3] Alan Kivitz,[4] MiJeong Kim,[5] Nino Joy,[5] Shoshanna Jiang,[5] Mary DiGiorgi,[5] Jonathan Slonin,[5] Derek Jackson[5]

[1]Metroplex Clinical Research Center, Dallas, TX; [2]University of Leeds, West Yorkshire, United Kingdom; [3]University of Maryland School of Medicine, Baltimore, MD; [4]Altoona Center for Clinical Research, Duncansville, PA; [5]Pacira BioSciences, Inc., Brisbane, CA

OBJECTIVE

To assess the impact of PCRX-201 on pain, stiffness, function, and immunogenicity in patients with knee osteoarthritis (OA) after 156 weeks

CONCLUSIONS

1. A single intraarticular (IA) injection of PCRX-201 with corticosteroid pretreatment in patients with knee OA had an acceptable safety profile and sustained clinical efficacy for up to 156 weeks
2. Preexisting neutralizing antibodies did not affect PCRX-201 efficacy or safety at all 3 doses
3. Corticosteroid pretreatment demonstrated greater improvement in clinical scores than no pretreatment
4. These results support the ongoing phase 2 study strategy of PCRX-201 with a 1.4×10^{10} viral genome copies (GC) dose (low dose in this phase 1b study) and 1.4×10^{11} viral GC dose (middle dose in this phase 1b study) alongside corticosteroid pretreatment

PRESENTING AUTHOR: Stanley Cohen; Stanley.Cohen@dfwra.com

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REFERENCES: 1. Deshpande et al. *Arthritis Care Res (Hoboken).* 2016;68(12):1743-1750. **2.** Buelt, Narducci. *Am Fam Physician.* 2021;103(2):120-121. **3.** Li et al. *Precis Clin Med.* 2023;6(2):pbad014. **4.** Senter et al. *Hum Gene Ther.* 2022;33(9-10):541-549.

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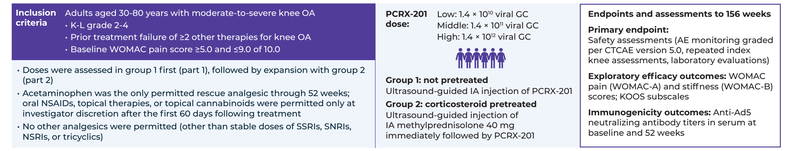
INTRODUCTION

- Knee OA is a common disease affecting ~15 million people in the United States[1]
- There is an urgent unmet need for additional OA treatments because current treatments provide only short-term pain relief and are often associated with adverse effects and contraindications[2]
- Gene therapy using viral vectors has emerged as a novel therapeutic modality with the potential to treat OA[3]
- PCRX-201 (enekinragene inzadenovec) is a novel high-capacity adenovirus (HCAd) serotype 5 vector carrying a transgene encoding for the inflammation-inducible expression of interleukin-1 receptor antagonist, currently under investigation to treat knee OA via IA injection[4]
- Data from an ongoing phase 1b study (NCT04119687) indicated that PCRX-201 was safe and associated with improvements in pain, stiffness, and function to the interim time point of 104 weeks, suggesting that PCRX-201 could potentially lead to reduced long-term pain and disability

METHODS

- This open-label phase 1b trial (NCT04119687) enrolled 2 groups (Figure 1)
  - Group 1: ultrasound-guided IA injection of PCRX-201 at low (1.4×10^{10} viral GC), middle (1.4×10^{11} viral GC), or high (1.4×10^{12} viral GC) dose
  - Group 2: same regimen and dosing, but preceded by IA methylprednisolone 40 mg to test whether immune modulation improved vector tolerability and transduction

Figure 1. Study design.



Ad, adenovirus; AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; GC, genome copies; IA, intraarticular; K-L, Kellgren-Lawrence; KOOS, Knee Injury and Osteoarthritis Outcome Score; NSAID, nonsteroidal anti-inflammatory drug; NSRI, nonselective serotonin reuptake inhibitor; OA, osteoarthritis; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

RESULTS

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

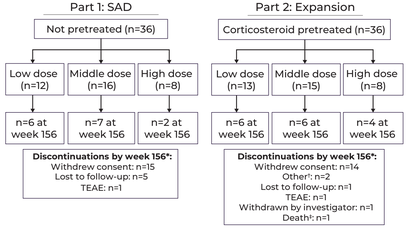
- 36 participants were enrolled and treated in each group (Figure 2)
- Participant demographics and baseline characteristics were similar across groups (Table 1)
  - Most participants were women (58%) with a Kellgren-Lawrence grade of 3 or 4 (81% in the not pretreated group and 83% in the corticosteroid pretreated group)
  - The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-A pain score was similar in both groups, and ~75% of participants had bilateral knee OA
- There was a similar number of discontinuations at week 156 in both groups (Figure 2)
  - At 156 weeks, 15 participants remained in the not pretreated group (8 discontinued between weeks 104 and 156) and 16 remained in the corticosteroid pretreated group (4 discontinued between weeks 104 and 156)

Table 1. Participant Demographics and Baseline Characteristics

	Not pretreated group (n=36)	Corticosteroid pretreated group (n=36)
Age, median (IQR), y	62.0 (58.5-67.0)	67.5 (58.5-71.5)
Women, n (%)	21 (58.3)	21 (58.3)
Race		
Asian	1 (2.8)	0
Black	4 (11.1)	4 (11.1)
White	31 (86.1)	32 (88.9)
K-L grade, n (%)		
2	7 (19.4)	6 (16.7)
3	23 (63.9)	15 (41.7)
4	6 (16.7)	15 (41.7)
WOMAC-A pain score, mean (SD)	6.4 (1.0)	6.8 (1.0)
BMI, mean (SD), kg/m²	32.1 (4.2)	31.2 (4.9)
Years since primary diagnosis, mean (SD)	8.6 (8.8)	14.6 (10.9)
Unilateral or bilateral knee OA, n (%)		
Unilateral	8 (22.2)	10 (27.8)
Bilateral	28 (77.8)	26 (72.2)
Follow-up, median (range), wk	142.5 (15, 156)	127 (8, 156)

BMI, body mass index; IQR, interquartile range; K-L, Kellgren-Lawrence; OA, osteoarthritis; SD, standard deviation; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Figure 2. Participant flow diagram.



*Some participants discontinued at week 156 after providing data; in those cases, week-156 data are included in the analysis. †One participant discontinued because of progression to total knee arthroplasty, and another participant did not continue in the extension after 104 weeks. ‡Not considered related to study treatment. SAD, single ascending dose; TEAE, treatment-emergent adverse event.

SAFETY

- **TEAEs:** the most commonly reported treatment-emergent adverse event (TEAE), index knee effusion, occurred less frequently in participants in the corticosteroid pretreated (15/36; 42%) than the not pretreated (24/36; 67%) group (Table 2)
- **Treatment-related TEAEs:** index knee effusion events were considered treatment-related TEAEs in 13 of 36 participants (36%) in the corticosteroid pretreated group and 22 of 36 participants (61%) in the not pretreated group
  - Among participants in the not pretreated group who had index knee effusion treatment-related TEAEs, 23% (5/22) were grade 1 (mild), 68% (15/22) were grade 2 (moderate), and 18% (4/22) were grade 3 (severe)
  - Among participants in the corticosteroid pretreated group who had index knee effusion treatment-related TEAEs, 8% (1/13) were grade 1 (mild), 85% (11/13) were grade 2 (moderate), and 8% (1/13) were grade 3 (severe)
  - Treatment-related index knee effusion TEAEs resolved in a median of 21 days in the not pretreated group (range, 2-165 days) and in a median of 22.5 days for the corticosteroid pretreated group (range, 3-111 days)

Table 2. Summary of TEAEs, SAEs, TEAEs Grade ≥3, and TEAEs Occurring in ≥10% of Participants in Any Pretreatment Group

	Not Pretreated			Corticosteroid pretreated		
	Low (n=12)	Middle (n=16)	High (n=8)	Low (n=13)	Middle (n=15)	High (n=8)
≥1 TEAE	11 (91.7)	16 (100)	8 (100)	12 (92.3)	14 (93.3)	8 (100)
≥1 SAE	3 (25)	1 (6.2)	1 (12.5)	1 (7.7)	2 (13.3)	2 (25)
≥1 TEAE grade ≥3	3 (25)	3 (18.8)	3 (37.5)	2 (15.4)	4 (26.7)	2 (25)
≥1 TEAE occurring in ≥10% of participants in either pretreatment group						
Joint effusion	6 (50)	10 (62.5)	8 (100)	5 (38.5)	5 (33.3)	5 (62.5)
Arthralgia	6 (50)	4 (25)	1 (12.5)	5 (38.5)	5 (33.3)	6 (75)
Joint swelling	7 (58.3)	1 (6.2)	1 (12.5)	0 (0)	2 (13.3)	0 (0)
Headache	2 (16.7)	1 (6.2)	2 (25)	1 (7.7)	2 (13.3)	1 (12.5)
Back pain	0 (0)	0 (0)	2 (25)	2 (15.4)	1 (6.7)	1 (12.5)
Fall	1 (8.3)	0 (0)	1 (12.5)	2 (15.4)	2 (13.3)	0 (0)
Osteoarthritis	0 (0)	0 (0)	0 (0)	1 (7.7)	2 (13.3)	3 (37.5)
Hypertension	2 (16.7)	2 (12.5)	0 (0)	1 (7.7)	0 (0)	0 (0)
Synovial cyst	3 (25)	1 (6.2)	1 (12.5)	0 (0)	0 (0)	0 (0)
Musculoskeletal pain	0 (0)	0 (0)	0 (0)	2 (15.4)	0 (0)	2 (25)

SAE, serious adverse event; TEAE, treatment-emergent AE. Data are the n (%), where n is the number of participants in each category. Participants who reported >1 TEAE are counted only once per category. n in the column headings is the number of participants in each steroid-pretreatment status and dose cohort and is the denominator for percentages.

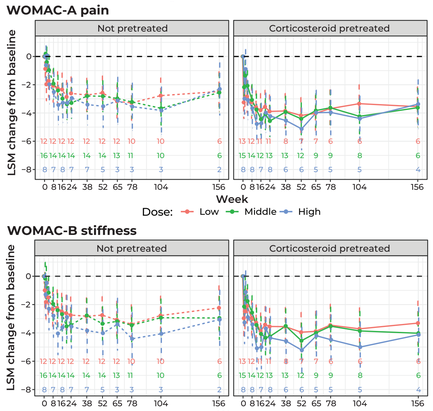
EFFICACY

- Improvements in pain and function were observed at all doses and across both the not pretreated and corticosteroid pretreated groups up to 156 weeks after PCRX-201 IA injection

WOMAC-A pain and WOMAC-B stiffness

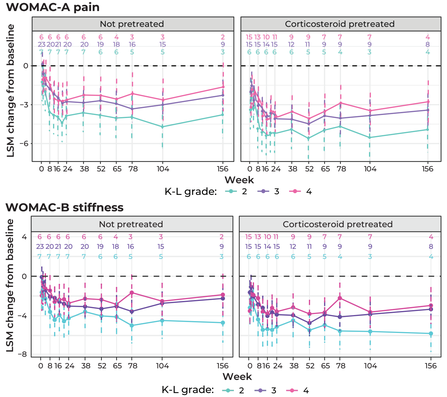
- The corticosteroid pretreated group demonstrated greater improvements for WOMAC-A pain versus the not pretreated group (range of least squares mean [LSM] reduction from baseline pain as observed across dose levels, 3.37-3.62 [of 10] points vs 2.30-2.55 points; Figure 3A)
- LSM improvements across the 3 doses were observed for WOMAC-B stiffness scores at 156 weeks in both the not pretreated group (2.23-3.06–point reduction from baseline stiffness as observed) and the corticosteroid pretreated group (3.31-4.13–point reduction from baseline stiffness as observed; Figure 3B)
- Participants in the pretreated group with K-L grade of 2, 3, and 4 showed LSM reductions from baseline in WOMAC-A pain (Figure 4A) and WOMAC-B stiffness (Figure 4B), with greater numerical reductions observed in those with K-L grade 2 than those with K-L grades 3 or 4

Figure 3. LSM change from baseline for WOMAC-A pain scores and WOMAC-B stiffness scores by dose.



The number of participants with WOMAC results may be different than enrollment totals because of participants still enrolled who did not attend the week-156 visit or participants who discontinued after attending the week-156 visit. Values in color are the sample size over time. Error bars are the 95% confidence interval. LSM, least squares mean; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Figure 4. WOMAC-A pain and WOMAC-B stiffness by K-L grade.

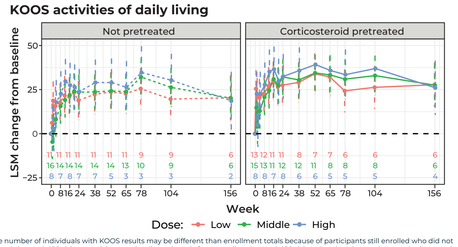


Values in color are the sample size over time. Error bars are the 95% confidence interval. K-L, Kellgren-Lawrence; LSM, least squares mean; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

FUNCTION

- **KOOS:** at 156 weeks, LSM improvements across the 3 doses were observed for Knee Injury and Osteoarthritis Outcome Score (KOOS) activities of daily living scores in both the not pretreated (range, 18.82-20.24 [of 100] points) and the corticosteroid pretreated group (range, 26.07-27.48 points; Figure 5)

Figure 5. LSM change from baseline for KOOS activities of daily living.

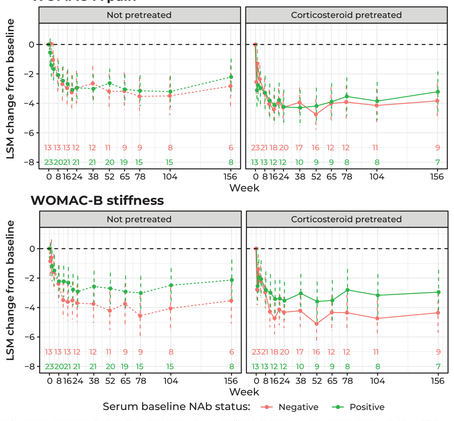


The number of individuals with KOOS results may be different than enrollment totals because of participants still enrolled who did not attend the week-156 visit or participants who discontinued after attending the week-156 visit. Values in color are the sample size over time. Error bars are the 95% confidence interval. LSM, least squares mean; KOOS, Knee Injury and Osteoarthritis Outcome Score.

IMMUNOGENICITY

- Importantly, preexisting serum neutralizing antibodies did not affect PCRX-201 efficacy as determined by WOMAC-A pain (Figure 6A) and WOMAC-B stiffness (Figure 6B)

Figure 6. LSM change from baseline for WOMAC-A pain scores and WOMAC-B stiffness scores by serum baseline NAb status.



Values in color are the sample size over time. Error bars are the 95% confidence interval. LSM, least squares mean; NAb, neutralizing antibody; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.