ABSTRACT NUMBER: 2760

A Phase 2 Double-Blind Clinical Trial to Examine the Comparative Effects on Osteoarthritic Knee Pain of CGS-200-1 (1% Capsaicin Topical Liquid), CGS-200-5 (5% Capsaicin Topical Liquid), and CGS-200-0 (Vehicle, No Capsaicin)

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Meeting: 2019 ACR/ARP Annual Meeting

Keywords: analgesics and drug therapy, Chronic pain, Knee, Osteoarthritis

SESSION INFORMATION

Date: Tuesday, November 12, 2019

Session Type: ACR Abstract Session

Session Title: 5T090: Osteoarthritis – Clinical II: Novel Therapies (2756–2761)

Session Time: 2:30PM-4:00PM

Background/Purpose: There is considerable unmet medical need for an osteoarthritic knee pain (OAKP) treatment that does not require regular daily use, does not carry gastrointestinal risk (e.g., NSAIDs), liver risk (e.g., acetaminophen) or addiction risk (e.g., opiates), and can safely provide long-lasting pain relief after a brief course of treatment. The Sponsor has clinically shown that topical OTC-strength 0.25% (w/w) capsaicin is well tolerated and provides OAKP relief. The Sponsor has now produced in the same vehicle (CGS-200) high potency, 5% (w/w) capsaicin (CGS-200-5) and 1% (w/w) capsaicin (CGS-200-1) topical products to evaluate as treatments for the relief of OAKP using the WOMAC subscales for pain, stiffness and function as well as total WOMAC score.

Methods: This was a multi-center, randomized (1:1:1), double-blind, parallel group, vehicle-controlled trial comparing topical CGS-200-1 or CGS-200-5 versus CGS-200-0 in 122 randomized subjects who had OA of at least one knee according to 1986 ACR criteria and a WOMAC pain score of ≥ 250. Subjects continued ongoing non-prohibited analgesic medication(s) (e.g., oral NSAIDs) at study entry with the expectation that the daily dose was to be maintained throughout the study if possible. Treatment was applied for 1 hour to both knees on 4 consecutive days (Study Days 1-4) by the subject under clinic supervision and then washed off. Clinical efficacy and safety assessments were made on Study Days 5, 19, 35 (the primary endpoint was Day 35 change in WOMAC pain score from baseline), 64, and 94. The modified intent to treat (mITT) subset of subjects was used for all efficacy analyses.

Results: CGS-200-5, but not CGS-200-1, met the primary Day 35 OAKP WOMAC pain efficacy endpoint compared to vehicle ($p = 0.020$, mITT population) and post-hoc analysis showed statistical separation from CGS-200-0 (Vehicle) on Days 64 ($p = 0.0001$) and 94 ($p = 0.0111$) **(Table 1)**. Post-hoc analysis showed a statistical difference in WOMAC OA total scores between both treatment groups and Vehicle at Days 35, 64 and 94 **(Table 2)**. The proportion of subjects with a durable clinical response (WOMAC pain reductions ≥ 50% on all study day visits minus one) was higher in the CGS-200-5 group at all visits **(Table 3)**. A slightly larger percentage of CGS-200-5 patients reported ≥ 1 TEAEs (all were mild or moderate in severity) compared to the CGS-200-0 or CGS-200-1 arms, with little difference

between groups in the types of TEAEs. Application site pain (mostly mild to moderate) was observed in all treatment groups, with a higher proportion of subjects in the CGS-200-5 group experiencing pain than the CGS-200-5 group. The mean tolerability AUCs in both active treatment groups decreased with each consecutive dosing day.

Conclusion: CGS-200-5 was well-tolerated and efficacious following application to both knees for 60 minutes on 4 consecutive days. Due to the significant efficacy and good safety and tolerability observed in this study, further clinical development of CGS-200-5 is warranted.

Table 1

Summary of WOMAC OA Pain Score Change from Baseline through Day 94 - mITT Set

Day	LSM Difference	Between Group Difference	95% CI[a]	p-value[a]
35	CGS-200-1 – CGS-200-0	-32.6	(-84.2, 19.0)	0.2137
64		-5.0	(-53.4, 43.3)	0.8366
94		-33.1	(-85.9, 19.7)	0.2171
35	CGS-200-5 – CGS-200-0	-61.0	(-112.3, -9.8)	0.0200
64		-94.7	(-142.4, -47.1)	0.0001
94		-67.0	(-120.0, -15.8)	0.0111

Abbreviations: LSM, Least-squares means; SD, standard deviation.

Notes: Only the assessment from "study knee" was included in the analysis.
Treatment success represents a reduction of at least 50% in WOMAC OA pain score from baseline. Subjects with missing data were considered a treatment failure for that visit.

Table 1

Table 1: Summary of WOMAC OA Pain Score Change from Baseline through Day 94 – mITT Set

Table 2

Summary of WOMAC OA Pain Score Change from Baseline through Day 94 Using AUC- mITT Set

Pain Score		CGS-200-0	CGS-200-1	CGS-200-5
Day 35				
Mean		-2385.1	-4060.4	-5289.0
SD		2557.78	3253.83	3308.18
Day 64				
Mean		-4914.1	-7065.8	-10067.1
SD		5270.18	5835.81	6094.49
Day 94				
Mean		-7246.8	-9770.9	-14677.7
SD		7861.64	8426.98	9108.35q
LSM Difference	**Day**	**Between Group Difference**	**95% CI[a]**	**p-value[a]**
CGS-200-1 – CGS-200-0	35	-1675.3	(-3048.5, -302.1)	0.0172
	64	-2151.7	(-4745.4, 443.0)	0.1032
	94	-2524.1	(-6381.0, 1332.8)	0.1974
CGS-200-5 – CGS-200-0	35	-2903.8	(-4268.4, -1539.2)	< 0.0001
	64	-5153.0	(-7714.6, -2591.4)	0.0001
	94	-7430.9	(-11236.7, -3625.2)	0.0002

Abbreviations: LSM, Least-squares means; SD, standard deviation.

Notes: Only the assessment from "study knee" was included in the analysis.
Treatment success represents a reduction of at least 50% in WOMAC OA pain score from baseline. Subjects with missing data were considered a treatment failure for that visit.
[a]ANCOVA model for comparison of change from baseline with treatment as a fixed effect and baseline value as a covariate

Table 2

Table 2: Summary of WOMAC OA Pain Score Change from Baseline through Day 94 Using AUC- mITT Set

Table 3

Summary of Durability of Clinical Response - mITT Set

Clinical Response Status	CGS-200-0 (N = 40)	CGS-200-1 (N = 40)	CGS-200-5 (N = 41)	Trend Test p-value[a]
Day 5				
Responder	7 (17.5%)	11 (27.5%)	19(46.3%)	
Non-responder	33 (82.5%)	29 (72.5%)	22(53.7%)	
Day 19				
Responder	7 (17.5%)	14 (35.0%)	21(51.2%)	
Non-responder	33 (82.5%)	26 (65.0%)	20(48.8%)	
Day 35				
Responder	11 (27.5%)	15 (37.5%)	19 (46.3%)	
Non-responder	29 (72.5%)	25 (62.5%)	22 (53.7%)	
Day 64				
Responder	9 (22.5%)	5 (12.5%)	23 (56.1%)	
Non-responder	31 (77.5%)	35 (87.5%)	18 (43.9%)	
Day 94				
Responder	10 (25.0%)	10 (25.0%)	18(43.9%)	
Non-responder	30 (75.0%)	30 (75.0%)	23(56.1%)	
Durable Clinical Response up to Day 35	6 (15.0%)	9 (22.5%)	15(36.6%)	0.0288
Durable Clinical Response up to Day 64	6 (15.0%)	4 (10.0%)	14(34.1%)	0.0365
Durable Clinical Response up to Day 94	5 (12.5%)	4 (10.0%)	12(29.3%)	0.0566
Comparison	**Day**	**Difference in Proportions (%)**	**95% CI [b]**	**p-value**
CGS-200-1 – CGS-200-0	35	7.5	(-15.5, 29.9)	0.5679
	64	-5.0	(-27.6, 18.0)	0.7370
	94	-2.5	(-25.2, 20.4)	1.0000
CGS-200-5 – CGS-200-0	35	21.6	(0.5, 42.4)	0.0415
	64	19.1	(-2.0, 40.1)	0.0703
	94	16.8	(-4.5, 37.8)	0.1004
CGS-200-5 – CGS-200-1	35	14.1	(-7.0, 35.6)	0.2246
	64	24.1	(3.0, 44.7)	0.0148
	94	19.3	(-2.0, 40.1)	0.0488

Notes: Only the assessment from "study knee" was included in the analysis.
Responder represents a reduction of at least 50% in WOMAC OA pain score from baseline. Subjects with missing data were considered a non-responder for that visit.
Percentages are based on the total number of mITT subjects in each treatment group (N).
Durable clinical response analysis is performed based on Section 6.3 in the SAP.

[a] Trend Test p-value was calculated using the Cochran-Armitage trend test.

[b] The 95% Confidence Interval (CI) of the difference in proportions and p-value are calculated using exact method.

Table 3

Table 3: Summary of Durability of Clinical Response – mITT Set

Disclosure: M. Billard, Vizuri Health Sciences, LLC, 3, 4; **J. Todhunter**, Vizuri Health Sciences, LLC, 3, 4; **M. Fleming**, Vizuri Health Sciences, LLC, 3, 4; **T. Warneke**, Vizuri Health Sciences, LLC, 3, 4; **Y. Qiu**, None; **N. Ly**, None; **W. Aronstein**, None; **W. Moore**, Vizuri Health Sciences, LLC, 1, 3, 4, 6.

To cite this abstract in AMA style:

Billard M, Todhunter J, Fleming M, Warneke T, Qiu Y, Ly N, Aronstein W, Moore W. A Phase 2 Double-Blind Clinical Trial to Examine the Comparative Effects on Osteoarthritic Knee Pain of CGS-200-1 (1% Capsaicin Topical Liquid), CGS-200-5 (5% Capsaicin Topical Liquid), and CGS-200-0 (Vehicle, No Capsaicin) [abstract]. *Arthritis Rheumatol.* 2019; 71 (suppl 10). https://acrabstracts.org/abstract/a-phase-2-double-blind-clinical-trial-to-examine-the-comparative-effects-on-osteoarthritic-knee-pain-of-cgs-200-1-1-capsaicin-topical-liquid-cgs-200-5-5-capsaicin-topical-liquid-and-cgs-200-0-v/. Accessed May 1, 2020.
