Preview Abstract

You have submitted the following abstract to 2017 ACR/ARHP Annual Meeting.

Click here to print this page now.

Reducing Heterogeneity in OA Clinical Trials: Data from a Phase 2 Study of SM04690, a Novel, Intra-Articular, Wnt Pathway Inhibitor in Knee Osteoarthritis

Program Book Publication:

Philip G. Conaghan, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds

Abstract Supplement and Online Publication:

These authors will be published in a supplement of the *Arthritis & Rheumatology* journal as well as the abstracts section of the ACR/ARHP Meeting Abstract website (acrabstracts.org).

Philip G. Conaghan[1], Anita DiFrancesco[2], Christopher J. Swearingen[2], Sarah Kennedy[2], Ismail Simsek[2], Jeymi Tambiah[2] and Yusuf Yazici[2], [1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, [2]Samumed, LLC

Abstract Text

Character count for abstract text: 2321 (429 Characters Remaining)

Background/Purpose: Kellgren-Lawrence [KL] radiographic grading is used to classify knee osteoarthritis (OA), but may not accurately reflect disease progression. Classifying subjects by baseline medial joint space width (mJSW) may be a more specific measure. This hypothesis was assessed in a post-hoc analysis of data from a phase 2, multicenter, 52-week, randomized controlled trial of SM04690, a small molecule Wnt pathway inhibitor in development as a potential disease modifying drug in knee OA.

Methods: In the trial, subjects with KL grade 2-3 knee OA were randomized to a single, 2 mL, intra-articular injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or placebo (PBO) into their target (most painful) knee at Day 0. WOMAC Pain and Function were assessed at 0, 4, 13, 26, 39 and 52 weeks, with fixed location radiographic assessment of mJSW at Weeks 0, 26 and 52. Exploratory analysis of clinical outcomes in the intention to treat (ITT) population was conducted by analysis of covariance adjusted for baseline mJSW with multiple imputation. This post-hoc analysis examined a group with baseline mJSW of 2-4 mm in comparison to the full ITT population.

Results: 455 subjects (mean age 60.3 [±8.7] years, BMI 29.9 [±4.6] kg/m^2, 268 [58.9%] female, 293 [64.4%] KL Grade 3) were enrolled. Contralateral knee KL grade was equal or worse than target knee in 91% of ITT population. 258 subjects had baseline mJSWs of 2-4 mm. At week 52, in the placebo group, imputed mean mJSW change from baseline was -0.14 [SE 0.06] mm. In the ITT population, compared to placebo, imputed mean mJSW changes from baseline were positive for 0.03 mg and 0.07 mg SM04690 doses (**Table, figure**). In the post-hoc analysis of the smaller 2-4mm mJSW subgroup, heterogeneity was similar to ITT for all doses compared to PBO and for the 0.03 mg and 0.07 mg doses changes beyond measurement error (>0.13 mm)[1] were observed. In addition, improvement in WOMAC Function compared to placebo was seen in the 0.07 mg SM04690 group at Week 52 within the mJSW subgroup (change compared to placebo -13.6, 95% CI (-25.5, -1.7), P=0.025).

Conclusion: Stricter inclusion criteria for mJSW provided a less heterogenous baseline group, reducing sample size by 42% without increasing standard error. When applied to this dataset, meaningful radiographic changes were demonstrated with 0.03 mg and 0.07 mg SM04690 groups compared to placebo. Future trials of structure modification in knee OA should consider specific mJSW inclusion criteria.

[1]Dupuis et al. OAC 2003

Table. mJSW Measurements for ITT and Baseline mJSW 2-4 mm subgroup

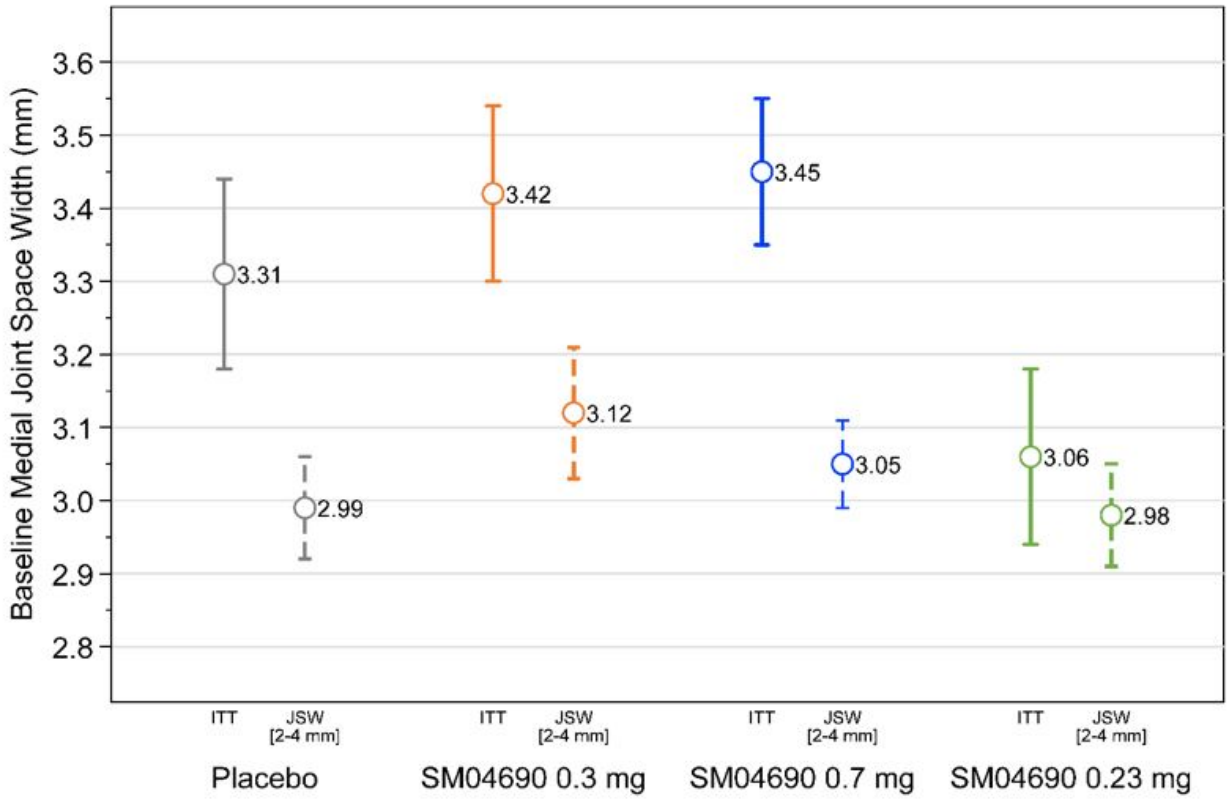
ITT

mJSW*	0.03 mg	0.07 mg	0.23 mg	PBO
N	112	117	110	116
Baseline (mm) Mean (SE)	3.42 (0.12)	3.45 (0.10)	3.06 (0.12)	3.31 (0.13)
Change at Week 52	-0.04 (0.06)	-0.09 (0.06)	-0.16 (0.07)	-0.14 (0.06)
Change compared to Placebo	0.10 (0.09)	0.06 (0.09)	-0.02 (0.09)	
P-value	*P*=0.259	*P*=0.529	*P*=0.807	

Baseline mJSW 2-4 mm

mJSW*	0.03 mg	0.07 mg	0.23 mg	PBO
N	56	72	65	65
Baseline	3.12 (0.09)	3.05 (0.06)	2.98 (0.07)	2.99 (0.07)
Change at Week 52	-0.03 (0.08)	-0.03 (0.08)	-0.16 (0.09)	-0.22 (0.09)
Change compared to Placebo	0.19 (0.13)	0.19 (0.12)	0.06 (0.13)	
P-value	*P*=0.144	*P*=0.121	*P*=0.624	

*Mean (SE) mJSW reported.



Disclosure: P. G. Conaghan, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 5, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 8;**A. DiFrancesco**, Samumed, LLC, 3, Samumed, LLC, 1;**C. J. Swearingen**, Samumed, LLC, 3, Samumed, LLC, 1;**S. Kennedy**, Samumed, LLC, 3, Samumed, LLC, 1;**I. Simsek**, Samumed, LLC, 3, Samumed, LLC, 1;**J. Tambiah**, Samumed, LLC, 3, Samumed, LLC, 1;**Y. Yazici**, Samumed, LLC, 3, Samumed, LLC, 1.

Topic Selection:

Osteoarthritis – Clinical Aspects

Submitter's E-mail Address:
sarahk@samumed.com

Preferred Presentation Format:
No Preference

Study Sponsors:

- Samumed: Samumed, LLC designed, funded and monitored the study. Samumed also conducted data management, and statistical analysis.

Keywords:
Knee, WNT Signaling, clinical trials, osteoarthritis and radiography

---

Additional Information:

Research Method:
Clinical

Trial Type:
Treatment

This abstract reports the results of a clinical trial not yet approved by a regulatory agency.

Trial Phase:
Phase II

Payment Received:
printable receipt
Confirmation Number:
acr-2017-6078-1547-8612-2355
Total Paid:
$70.00

We have agreed to the following statements:

I. I affirm that I have read and agree to the ACR/ARHP Annual Meeting general guidelines and policies for abstract submission outlined in the 2017 Call for Abstracts guidelines.
II. I affirm that any work with human or animal subjects reported in the abstract complies with the guiding principles for experimental procedures found in the Declaration of Helsinki of the World Medical Association.
III. I understand that case reports and reviews of literature are not appropriate and will not be reviewed.
IV. I understand that if the abstract reports the results of a clinical trial not yet approved by a regulatory agency, the trial phase must be indicated on the submission form.
V. I understand that an abstract is ineligible for consideration if it reports work that has been accepted for publication as a manuscript prior to the ACR/ARHP submission deadline of Monday, June 19, 2017.
VI. I understand that this abstract, if accepted, will be under embargo until 4:30 PM Eastern Time on Saturday, November 4, 2017.
VII. I understand that abstracts submitted for the ARHP may not be dually submitted to the ACR and vice versa.
VIII. I understand that, if accepted, the American College of Rheumatology has permission to publish this abstract in printed and/or electronic formats.

IX. I understand that, if accepted for presentation, the presenting author or co-authors listed on the abstract must present the abstract during an oral and/or poster presentation.
X. I affirm that this abstract title does not include a trial group name or acronym and understand that the ACR/ARHP will no longer publish them.
XI. I affirm that this abstract does not report results that have been previously presented at an ACR/ARHP Annual Meeting.

First Author

Presenting Author
Philip G. Conaghan, MD, PhD
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds
Leeds,
United Kingdom
Phone Number: 44-113-392-4884
Email: p.conaghan@leeds.ac.uk -- Will not be published

* ACR Member
* Membership Number 34389

Biographical Sketch: Philip Conaghan is Professor of Musculoskeletal Medicine at the University of Leeds; Honorary Consultant Rheumatologist for the Leeds Teaching Hospitals NHS Trust; and Deputy Director of the NIHR Leeds Biomedical Research Centre. He served as Chair of the national Arthritis Research UK Osteoarthritis and Crystal Disorders Clinical Studies Group for the last decade and is a former Chair of the NICE OA Guidelines Development Group. On an international level, he serves as co-executive lead of OMERACT; he is also a past-President of the International Society for Musculoskeletal Imaging in Rheumatology, and was Inaugural Chair of the EULAR Standing Committee on Musculoskeletal Imaging. Dr. Conaghan has secured over £50 million in personal and collaborative grant income. He has been an invited speaker at EULAR and ACR annual meetings for the past 10 years, serves on a number of editorial boards of leading rheumatology journals, and is current co-editor of the Oxford Textbook of Rheumatology. He has authored over 400 Pubmed listed publications, cited over 15,000 times.

Click to view Conflict of Interest Disclosure

Author Classification: Not applicable (Non-Trainee)

Second Author

Anita DiFrancesco
Samumed, LLC
San Diego, CA
Email: anita@samumed.com -- Will not be published

Click to view Conflict of Interest Disclosure

Third Author

Christopher J. Swearingen, PhD
Samumed, LLC
San Diego, CA
Email: chris@samumed.com -- Will not be published

Click to view Conflict of Interest Disclosure

Fourth Author

Sarah Kennedy, PhD
Samumed, LLC
9381 Judicial Dr.

San Diego, CA
Email: sarahk@samumed.com -- Will not be published

Click to view Conflict of Interest Disclosure

Author Classification: Not applicable (Non-Trainee)

Fifth Author

Ismail Simsek, MD
Samumed, LLC
San Diego, CA
Email: ismail@samumed.com -- Will not be published

Click to view Conflict of Interest Disclosure

Sixth Author

Jeymi Tambiah, BSc, MBChB, FRCS, MD
Samumed, LLC
San Diego, CA
Email: jeymi@samumed.com -- Will not be published

Click to view Conflict of Interest Disclosure

Seventh Author

Yusuf Yazici, MD
Samumed, LLC
San Diego, CA
Email: yusuf@samumed.com -- Will not be published

Biographical Sketch: Dr. Yazici is an internationally-renowned rheumatologist, researcher, and an expert in clinical trial design and management. He is a Clinical Associate Professor at NYU and the Director of Seligman Center for Advanced Therapeutics, which conducts all clinical trials in rheumatology at the NYU Hospital for Joint Diseases. Dr. Yazici is also the Director of Behcet's Syndrome Center, the largest center for Behcet's Disease in the US. He has published more than 250 medical papers and book chapters, and has given numerous national and international presentations. Dr. Yazici completed his Fellowship in Rheumatology at the Hospital for Special Surgery of Weill Medical College of Cornell University in New York and Residency in Internal Medicine at Creighton University in Nebraska. Dr. Yazici received his medical degree from Istanbul University.

Click to view Conflict of Interest Disclosure

If necessary, you can make changes to your abstract submission

- To access your submission in the future, use the direct link to your abstract submission from one of the automatic confirmation emails that were sent to you during the submission.
- *Or* point your browser to /acr/reminder.cgi to have that URL mailed to you again. Your username/password are 67292 / 999562.

Any changes that you make will be reflected instantly in what is seen by the reviewers. You DO NOT need to go through all of the submission steps in order to change one thing. If you want to change the title, for example, just click "Title" in the abstract control panel and submit the new title.

When you have completed your submission, you may close this browser window.

Tell us what you think of the abstract submittal

Home Page