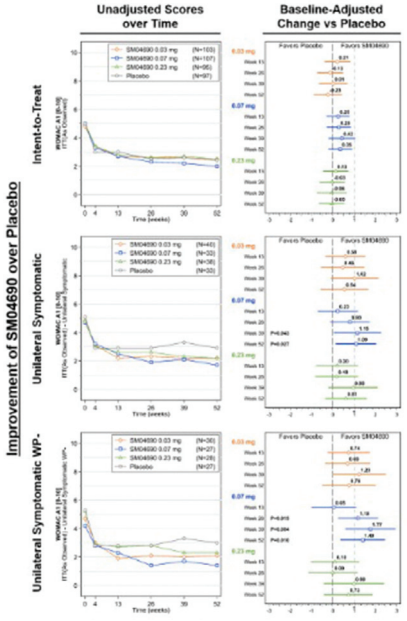
signalling is involved in these cellular processes. SM04690, a small molecule, intra-articular (IA), Wnt pathway inhibitor, is in development for treatment of knee OA as a potential disease modifying drug.

Objectives: A phase 2, multicenter, 52 week, randomised, double-blind, placebo-controlled (PBO) trial of SM04690 was conducted. Safety and efficacy outcomes including the Western Ontario and McMaster Universities Arthritis Index (WOMAC) question A1 were evaluated.

Methods: Subjects with ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2–3, received a single 2 mL IA injection of SM04690 (0.03, 0.07 or 0.23 mg) or PBO in the target (most painful) knee. WOMAC was assessed at baseline and 4, 13, 26, 39 and 52 weeks post-injection. WOMAC question A1, ('how much pain have you had when walking on a flat surface?'), was analysed as an exploratory outcome. Analysis of covariance adjusted for WOMAC A1 baseline in the intent-to-treat (ITT) population was conducted. Two subgroups identified in the primary analysis[1] were also explored: 1) subjects with unilateral symptomatic knee OA (pre-specified) and 2) subjects with unilateral symptomatic knee OA without widespread pain or comorbid symptoms (Widespread Pain Index≤4 and Symptom Severity≤2 [WP-], post-hoc).



Abstract OP0061 – Figure 1. Change and ladder plots deploting average WOMAC A1 improvement in SM04690 over placebo adjusted for baseline WOMAC A1. *Minimal clinicaly improvement difference (MCID) difined as 10% of WOMAC A1.

Results: 455 subjects, mean age 60.3 [±8.7] years, BMI 29.9 [±4.6] kg/m^2, female 58.9%, KL 3 [64.1%], with unilateral symptomatic OA [36.0%]) were enrolled (n=402 [88.4%] completers). No safety signals were observed.

For WOMAC A1, in the ITT population, no statistically significant differences between treatment groups and PBO were seen, although the 0.07 mg dose demonstrated improvements compared to PBO at all timepoints (figure 1). In unilateral symptomatic subjects, 0.07 mg showed statistically significant improvements in WOMAC A1 compared to PBO at Weeks 39 (-1.2, 95% CI: [−2.3 to −0.0], p=0.043) and 52 (-1.1, 95% CI: −2.0 to −0.1, p=0.027).

In unilateral symptomatic WP- subjects, the 0.07 mg dose showed statistically significant improvements in WOMAC A1 compared to PBO at Week 26 (-1.2, 95% CI: −2.1 to −0.2, p=0.015), through Weeks 39 (-1.8, 95% CI: −3.0 to −0.6, p=0.004) and 52 (-1.4, 95% CI: −2.5 to −0.4, p=0.010).

Conclusions: In this phase 2 study, improvements compared to PBO in WOMAC A1 were seen in clinically relevant unilateral symptomatic and unilateral symptomatic WP- subgroups. The improvements seen in this combined, multi-dimensional outcome of pain and function suggested SM04690 has a potential role in the treatment of signs and symptoms of knee OA.

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[1] Yazici Y, et al. *Arthritis Rheumatol* 2017;69(Suppl S10):935.

Disclosure of Interest: S. Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, H. Ghandehari Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Hochberg Consultant for: Bioberica, EMD Serono, Novartis Pharma AG, Plexxikon, Pfizer, Proximagen, Regeneron, Samumed, LLC, Theralogix LLC

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LB0002

BIOMECHANICAL THERAPY FOR OSTEOARTHRITIS OF THE KNEE: A RANDOMISED CONTROLLED TRIAL (BIOTOK)

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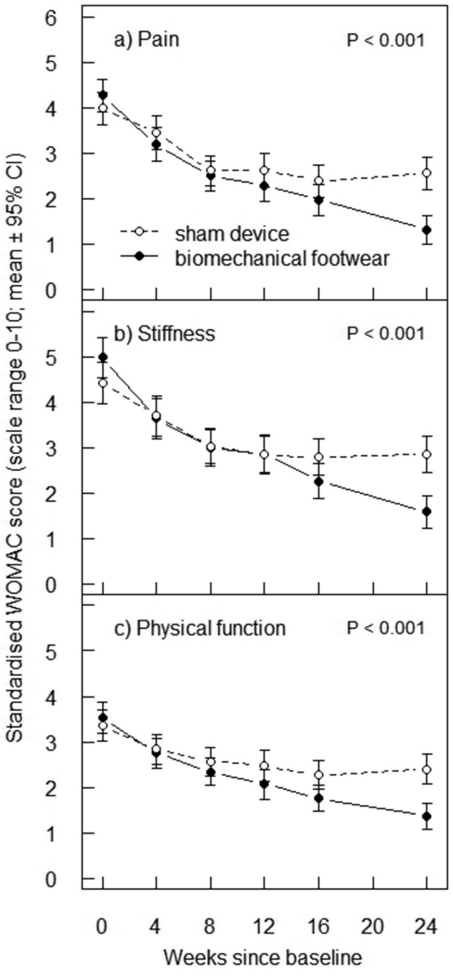
Background: Biomechanics plays an important role in knee osteoarthritis (OA). A new biomechanical footwear system aims at altering knee loading patterns and retraining neuromuscular control of the lower extremities. It consists of shoes with two adjustable convex pods at the soles, which are adjusted based on gait analysis, with the hypothesis that adjustments of the location of the pods will alter limb biomechanics so as to unload diseased compartments of the knee and that walking on the convex pods will facilitate muscular retraining.

Objectives: The aim of this trial was to compare the efficacy and safety of the new biomechanical footwear with an identical appearing shoe with flat pods (the sham device) in relieving pain and improving physical function in patients with knee OA.

Methods: In this randomised sham-controlled trial, patients with radiological knee OA (Kellgren-Lawrence grade ≥2), knee pain lasting for ≥6 months, and moderate pain on the WOMAC pain subscale (≥3 on a standardised scale from 0 to 10) were randomly assigned 1:1 to the biomechanical footwear or the sham device. The same shoe or device was provided for bilateral use. Patients in both groups were instructed to use the footwear for 30 minutes/day during the first week, and to increase use by 10 minutes/day each week to a maximum of 5 hours/day at 24 weeks. After 4, 8, 12, and 16 weeks, each patient's footwear



Abstract LB0002 – Figure 1

was re-calibrated by technicians. Because the sham device had no adjustable pods on the soles, technicians pretended to make appropriate changes.
The primary endpoint was knee pain at the end of treatment in the knee with more pain at screening, assessed with the WOMAC pain subscale. Secondary outcomes were WOMAC physical function and stiffness subscales. All subscales were standardised to range from 0 to 10. These outcomes were analysed using linear models adjusted for baseline values and the two stratification factors uni- vs. bilateral, and medial vs. lateral osteoarthritis at randomization, using multiple imputation.
Results: Of 697 patients assessed for eligibility, 220 were randomised: 111 to the experimental footwear and 109 to the sham device. The mean age was 65.2 years (SD 9.2) and the mean body mass index was 28.0 (SD 4.6). Overall, 47.3% were women and 88.2% had medial knee OA in the index knee. The mean WOMAC pain score at baseline was 4.1 (SD 1.9). Seven patients in the experimental group and 13 in the sham group dropped out. At the end of the trial, the adjusted mean difference for WOMAC pain was 1.34 (95% CI: 0.92 to 1.77) in favour of the experimental footwear. The adjusted mean difference was 1.42 (0.93 to 1.91) for WOMAC stiffness and 1.12 (0.73 to 1.50) for WOMAC physical function (figure 1). Three serious adverse events occurred in the experimental group, compared with 9 in the sham group; none were treatment-related. Thirty adverse events occurred in the experimental group, compared with 36 in the sham group; 18 and 17 of these, respectively, were possibly treatment-related.
Conclusions: This trial suggests that the new biomechanical footwear system is both efficacious and safe in relieving knee pain in patients with knee OA.
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WEDNESDAY, 13 JUNE 2018

Fracture risk and consequences

OP0062 OSTEOPOROTIC HIP FRACTURES IN MEN: A RISING CONCERN

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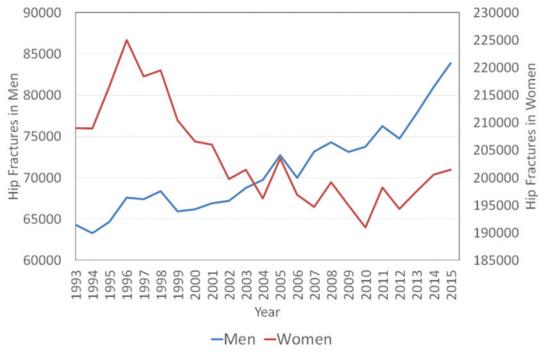
Background: Osteoporosis screening and treatment is often exclusively targeted at post-menopausal women. The US Preventive Task Force guidelines recommend bone density screening in women starting at age 65, but do not make any similar recommendation for men, even though men have higher mortality than women after a hip fracture.[1] Recent improvements in health care has led to increasing lifespan of men in US. As more men enter the seventh and eighth decades of their life, they are at more risk for developing osteoporosis and osteoporotic hip fractures.
Objectives: To study the number and prevalence of hospitalizations for osteoporotic hip fractures in the men and women aged 50 years and up in the US over 23 years (1993–2015).
Methods: The National Inpatient Sample (NIS) is a stratified random sample of all US community hospitals and is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2015 with a primary diagnosis of non-traumatic (osteoporotic) hip fractures in individuals 50 years and older. Patients were excluded if there was any evidence of major trauma, open fractures, or primary or secondary femoral tumours. US population estimates and projections for the resident US population were obtained from the US Census Bureau. All prevalence rates were expressed per 1 00 000 of the US population.
Results: From 1993 to 2015, we studied 6.3 million osteoporotic hip fracture hospitalizations in 1.99 billion person-years of observation in individuals who were 50 years or older. Of these,74% occurred in women. Hip fracture hospitalizations in women decreased from 2 09 052 in 1993 (prevalence 562 per 1 00 000 person-years) to 2 01 435 in 2015 (340 per 1 00 000 person-years), even as the population of 50 years and older women increased from 37 million in 1993 to 59 million in 2015 (59% increase in population), perhaps reflecting increasing awareness, screening and treatment for osteoporosis in elderly women. However, in men aged 50 years and older, osteoporotic hip fracture hospitalizations increased from 64 339 in 1993 to 83 885 in 2015, even as the prevalence decreased from 218 per 1 00 000 person-years in 1993 to 162 per 1 00 000 person-years in 2015. The 30% increase in the absolute number of hip fracture hospitalizations, despite decreasing prevalence, is coincident with the 75% rise in the number of the 50 years and older men population, from 29.6 million in 1993 to 51.7 million in 2015.



Abstract OP0062 – Figure 1. Hip fracture hospitalisation in the US

Conclusions: Despite an overall decrease in prevalence, the absolute number of osteoporotic hip fracture hospitalizations increased in 50 years and older men. More attention needs to be paid to prevention of osteoporotic hip fractures in this cohort.

REFERENCE:
[1] Hawkes WG, et al. Gender differences in functioning after hip fracture. J Gerontol A Biol Sci Med Sci 2006;61(5):495–9.

Disclosure of Interest: None declared
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OP0063 PERIPHERAL ARTERIAL DISEASE AND RISK OF OSTEOPOROTIC HIP FRACTURE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COHORT STUDIES

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Background: Previous studies have demonstrated that patients with peripheral arterial disease (PAD) had lower bone mineral density, particularly in the femur, compared with general population. Therefore, it is possible that patients with PAD may have a higher risk of osteoporotic hip fracture.
Objectives: To compare the risk of developing hip fracture between patients with PAD and individuals without PAD.
Methods: A systematic literature search was conducted using EMBASE and MEDLINE database from inception to November 2017 to identify all cohort studies that investigated the risk of incident hip fracture among patients with PAD compared with individuals without PAD. The systematic literature review was independently conducted by the first two investigators using the search strategy that included the terms for 'peripheral arterial disease' and 'hip fracture'. Eligible studies must be cohort studies (either prospective or retrospective) that reported the risk of incident hip fracture among patients with PAD. Comparators must be individuals without PAD. Eligible studies must provide the effect estimates (relative risks (RR) or hazard ratios (HR)) with 95% confidence intervals (CI) for the calculation of pooled effect estimates. Adjusted point estimates from each study were combined togetehr using the random-effect, generic inverse variance method as described by DerSimonian and Laird.
Results: Of 8464 retrieved articles, 6 cohort studies (3 prospective cohort studies and 3 retrospective cohort studies) involving 15 895 patients with PAD and 2 33 835 comparators without PAD met the eligibility criteria and were included in the meta-analysis. We found a significantly increased risk of incident hip fracture among patients with PAD compared with individuals without PAD with the pooled RR of 1.64 (95% CI: 1.17 to 2.29). The statistical heterogeneity was high with an I^2 of 80%. Subgroup analysis by study design showed a significantly increased risk of incident hip fracture among patients with PAD for both prospective studies (pooled RR 1.60; 95% CI: 1.12 to 2.28; $I^2$0%) and retrospective studies (pooled RR 1.72; 95% CI: 1.07 to 2.77; $I^2$92%) as shown in figure 1.