EXCITING NEW STUDY AIMS TO EXPLORE FURTHER AND DETERMINE MORE CLEARLY HOW A PIONEERING TREATMENT FOR KNEE OSTEOARTHRITIS '*WORKS*' IN THE NHS

Patient trial also has potential to improve understanding around which patients are most likely to benefit from the novel hydrogel, Arthrosamid®

A major new study to confirm the clinical effectiveness of a novel treatment for knee osteoarthritis in a UK setting is underway at The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust (RJAH).

Funded by non-biodegradable hydrogel pioneers, Contura Orthopaedics, with a research grant of over £150,000, this first study of its kind in the UK aims to determine the pathways on which Contura's minimally invasive treatment, the 2.5 iPAAG* single injection Arthrosamid® [based on 97.5% water and 2.5% cross-linked polyacrylamide] acts when used to treat patients with knee osteoarthritis (OA) by detecting the changes which occur in the joint after the injection is administered.

In the UK, approximately 4.11 million people are affected by knee OA, which causes discomfort, chronic pain and mobility issues. The economic burden of the condition to the NHS is significant. The estimated annual direct cost of physical inactivity to the NHS across the UK is £1.06 billion and the related NHS costs associated with obesity total £6.1 billion[1]. The burden of joint disease not only includes physical problems but it also has a negative effect on mental health. In fact, psychological distress is more frequently experienced by patients with OA compared to patients with diabetes. As such, physical and psychological impairment leads to a significant socioeconomic burden secondary to missed work days and disability. OA results in loss of economic production of over £3.2 billion per year, £215 million is spent on social services and £43 million on community services[2].

Effective treatment in this patient group can reverse these symptoms and consequently have a substantial positive effect on society.

Prior to surgical intervention, the conservative treatment of knee osteoarthritis involves pain relief medication and intra-articular injections. Currently, only steroid injections are available as part of NHS treatment, which are widely recognised as only having a short-term benefit, with potentially detrimental effects on residual cartilage.

Chief Investigator, Professor Martyn Snow, Consultant Orthopaedic Surgeon, at The RJAH will oversee the research project, monitoring the 60 patients with knee OA, considered by their consultant as requiring non-surgical treatment, who have been recruited into the trial.

*intra-articular polyacrylamide hydrogel injection (iPAAG)

Professor Snow explains; "It is very important that we determine how novel therapies such as Arthrosamid work. This will enable us to potentially identify patients who will benefit the most from the treatment and consequently improve the overall response rate. In this way we can maximise the cost-effectiveness of the treatment, facilitating access within the NHS. The response to the trial has been phenomenal and we have been contacted by patients and doctors all around the country. We have already recruited all the patients required to undertake the study and we hope to complete all the required injections by November 2023. I think this collaboration with our research group perfectly demonstrates how the NHS and Universities can work with industry to the benefit our patients."

For over two decades, iPAAG has shown huge promise as an injectable therapy for joint osteoarthritis. Initial studies in horses demonstrated impressive sustained results after two years of follow up. In a series of clinical trials over the last 10 years Arthrosamid® has demonstrated improved function and reduced pain in human knees. New data first released at the Annual Congress of Osteoarthritis Research International in March 2023, highlighted impressive 3-year results, showing that a single injection of 6 ml 2.5% polyacrylamide hydrogel, Arthrosamid®, continued to be "well-tolerated and demonstrated clinically relevant and statistically significant effectiveness in reducing pain, 3 years after treatment[3]".

In all trials to date, Arthrosamid® has been shown to have no serious adverse events, with any device related events mild and transient in nature[4]. A growing number of anecdotal cases in Denmark report that many patients, 5-8 years post treatment are still experiencing positive effects.

However, whilst the benefits in terms of pain and function have translated impressively well from 'horses to humans', the mode of action by which the injectable acts warrants further research.

Contura International's CEO Rakesh Tailor, comments; "We are aware, both anecdotally and through a growing body of evidence-based research, of the significant benefits of Arthrosamid® in terms of improved pain and function. There is of course though always more to be learnt about the pathways by which our hydrogel physically acts.

"We are therefore both delighted and excited to be funding this new study, the aim of which is to learn more about the mechanisms of action, as well as helping to gain a better understanding of the potential markers which will allow clinicians to predict a good clinical response in patients.

"And, once armed with this new evidence and insight into patient outcome, we can pave the way for further conversations around making the treatment more widely available within the NHS."

On entering the trial, baseline outcome measures will be recorded. The level of knee pain will be evaluated using Visual Analogue Scale (VAS). Patients will also be asked to complete the Knee injury and Osteoarthritis Outcome Score (KOOS) score and Western Ontario and McMaster Universities Arthritis Index (WOMAC). Patients will also declare the quantity of anti-inflammatory drugs and oral analgesia that they have used to help manage their pain. They will be followed up initially to 12 months and then to 5 years post injection or to Total Knee Replacement surgery, whichever is first.

Lead researcher, Dr Karina Wright explains; "Our approach is to sample the synovial fluid in patients receiving the treatment. Synovial fluid, the slippery fluid that bathes the knee cartilage and helps to provide the frictionless movement seen in healthy knee joints, has been shown to reflect changes in the joint. So, for example, if the lining of the joint is inflamed, the synovial fluid will contain more pro-inflammatory proteins. As such, the synovial fluid can provide vital information on the biological activity in several of the knee joints tissues and structures. By measuring the proteins present in the synovial fluid pre- and post- Arthrosamid® treatment, we will start to gain insight into the physical action of the iPAAG and perhaps also which patients are most likely to benefit."

Ends

For further information or to interview a spokesperson from Contura Orthopaedics Ltd about the current trail with the RJAH NHS Trust, please contact Jo Hudson on 0770 948 7959 / 020 7112 4905 or email jo.hudson@trinitypr.co.uk

For more information about the treatment and how to access Arthrosamid (in a network of clinics across the UK) and to review available clinical evidence, visit www.arthrosamid.com

Notes to editors:

About the trial: The approach used to measure the protein changes in the synovial fluid will combine state-of-the-art analysis techniques called proteomics and bioinformatics, which quantitate all of the proteins detectable in a sample using mass spectrometry and look at their functions together using

specialist computer-based libraries and software. In addition, targeted approaches will be used to look for specific proteins of interest, considered likely to inform the research team about potential modes of action or that have provided predictive value in other similar studies. Together this approach will provide the most comprehensive view on what is changing biologically in the joint as a result of the physical action of Arthrosamid® on the synovial tissue.

About Arthrosamid®: In April 2021, Arthrosamid® received CE mark as a medical device (European market approval) for the symptomatic treatment of patients with knee osteoarthritis (OA), following the completion of a twelve-month prospective open label study[5] which saw patients experience significant pain reduction. The CE mark for Arthrosamid® represented a major milestone for a product that has been in development for more than 20 years and fulfils an unmet clinical need for an effective, long-acting, safe and minimally invasive treatment that may postpone and potentially prevent knee surgery for those with OA[6].

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