News & Views in ...

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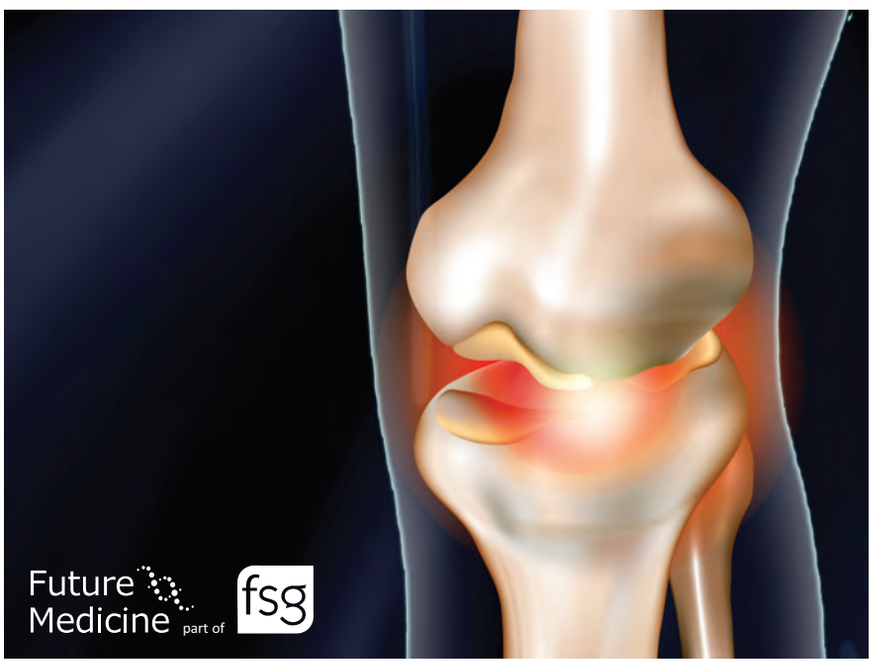
Highlighting the latest news in clinical rheumatology

Roche receives EU approval for new subcutaneous formulation of RoACTEMRA

Roche (Basel, Switzerland) has recently announced that the subcutaneous formulation of RoACTEMRA (tocilizumab) has received approval from the European Commission for the treatment of moderate to severe rheumatoid arthritis (RA) in patients who are either intolerant to or have failed to respond to other RA treatments. The approval makes RoACTEMRA the first anti-IL-6 receptor biologic available as subcutaneous and intravenous (iv.) formulations for both monotherapy and combination therapy with methotrexate (MTX).

Discussing the approval Sandra Horning, Head of Global Product Development and Chief Medical Officer at Roche, commented: "Today's European approval of RoACTEMRA is important because it provides physicians and patients with the flexibility to choose a treatment method that suits their needs. Together with their physicians, patients can choose whether to self-inject RoACTEMRA at home or have it administered in their doctor's office."



The approval was based on data from the Phase III SUMMACTA and BREVACTA studies. SUMMACTA demonstrated that the efficacy and tolerability of subcutaneous RoACTEMRA was comparable with intravenous RoACTEMRA. In addition, subcutaneous RoACTEMRA demonstrated long-term efficacy and reduced progression of joint damage over 48 weeks compared with placebo in the BREVACTA study. The subcutaneous formulation of RoACTEMRA will be available via a prefilled syringe.

The extensive RoACTEMRA clinical development program included five Phase III clinical studies and enrolled more than 4000 people with RA in 41 countries. In addition, the Phase IV ADACTA study showed that monotherapy with RoACTEMRA iv. was superior to monotherapy with adalimumab in reducing signs and symptoms of RA in MTX-intolerant patients or patients for whom MTX treatment was considered ineffective or inappropriate. The overall safety profile of both medications was consistent with previously reported data. These data were recognized in the recent European League Against Rheumatism recommendations for the management of RA, where RoACTEMRA was recommended as a first-line biologic and was highlighted for use as monotherapy.

RoACTEMRA iv. formulation is also approved for the treatment of active systemic juvenile idiopathic arthritis (SJIA) and poly-

articular juvenile idiopathic arthritis (PJIA) in patients 2 years of age and older.

RoACTEMRA is part of a co-development agreement with Chugai Pharmaceutical. It has been approved in Japan since April 2005 for Castleman's disease, followed by approvals for RA, SJIA and PJIA in 2008. More than 275,000 patients have been treated with RoACTEMRA since it first launched. RoACTEMRA is approved in more than 100 countries worldwide including countries in the EU, the USA, China, India, Brazil, Switzerland and Australia. It is available in more than 90 of these countries.

Source: Roche press release: www.roche.com/media/media_releases/med-cor-2014-04-28.htm

New clues on tissue scarring in scleroderma

A recent discovery by scientists at Northwestern (IL, USA) may lead to potential new treatments for breaking the cycle of tissue scarring in people with scleroderma.

The findings reported by the team led by Swati Bhattacharyya (Northwestern) underlie the new potential therapeutic options. Discussing the study Bhattacharyya commented: "Our results show how a damage-associated protein called fibronectin (FnEDA) might trigger immune responses that convert normal tissue repair into chronic fibrosis in people with scleroderma. We also found that FnEDA, which is undetectable in healthy adults, was markedly increased in the skin biopsies of patients with scleroderma."

In order to investigate the connection between immunity and fibrosis in scleroderma, the team observed skin biopsies of scleroderma patients to identify factors responsible for persistent scarring and reported that FnEDA was highly elevated. In order to test the theory that FnEDA was needed for the scarring to occur, the researchers used a genetically engineered mouse lacking the protein and observed that these mice did not develop skin fibrosis. On a cellular level, FnEDA triggered an immune response in skin cells, leading to fibrosis. Moreover, a small molecule which specifically blocks the cellular immune response triggered by FnEDA was able to prevent skin fibrosis in mice.

"This pioneering study using state-of-the-art experimental approaches is the first to identify an innate immune pathway for scleroderma fibrosis," said Dr Varga, one of the study's authors. "We expect that the results will shift our thinking about the disease, and hopefully open new avenues for its treatment."

"We have raised the possibility for developing novel therapeutic approaches," Bhattacharyya added. "We are also developing novel small molecules to selectively block the receptor for FnEDA as a potential anti-fibrotic therapy in humans."

Source: Eureka press release: www.eurekalert.org/pub_releases/2014-04/nu-nco041714.php

Sprifermin may offer benefit for cartilage loss in knee osteoarthritis

A recently published study in patients with osteoarthritis (OA) of the knee has demonstrated that at 12 months, total femorotibial cartilage thickness loss was reduced in knees treated with sprifermin compared with placebo-treated knees. While OA is the most common cause of physical disability in older adults, studies suggest that the average age at diagnosis is 55 years. No medication or alternative treatment (glucosamine, chondroitin) has shown positive effects on preventing or reversing the structural changes of joint damage caused by OA.

The results suggested that sprifermin dosed at 100 μg reduced loss of cartilage thickness and volume in the total femorotibial joint and in the lateral knee compartment (outside of the knee). One of the researchers, researcher LS Lohmander (Lund University, Lund, Sweden), commented: "Currently, no structure-modifying treatment has been approved by US or EU regulatory bodies. Our trial investigates the safety and efficacy of sprifermin in preventing loss of cartilage due to OA in the knee."

The double-blind trial recruited 192 knee OA patients randomized to single-ascending doses intra-articular injection of sprifermin or placebo or to multiple-ascending doses of sprifermin or placebo. Doses of the drug were administered at 10, 30 and 100 μg.

The team measured cartilage thickness at 6 and 12 months using MRI, joint space width by x-ray, and pain was scored using the Western Ontario McMaster Universities (WOMAC) OA index.

At 12 months, researchers found no change in the thickness of cartilage in the central medial femorotibial compartment in patients injected with sprifermin. However, a reduction in loss of total and lateral femorotibial cartilage thickness and volume was noted in patients injected with 100 μg of sprifermin versus placebo. Narrowing of the joint space width was also reduced in the lateral femorotibial compartment for OA patients who received the same dose. The WOMAC pain score improved in all patients, with less improvement shown at 12 months for patients who received 100 μg sprifermin compared with placebo.

Dr Lohmander concluded: "While our trial found no reduction in cartilage thickness in the central femorotibial compartment among subjects in the treatment group, dose-dependent reductions in structural changes were found in participants treated with sprifermin." The authors found no safety or injection-site issues with sprifermin. Additional clinical studies will be needed to replicate these findings and confirm the optimal dosing.

Wiley press release: http://eu.wiley.com/WileyCDA/PressRelease/pressReleaseId-110650.html

Study identifies potential molecules involved in rheumatoid arthritis angiogenesis

Researchers from the University of Illinois (IL, USA) have published a study suggesting that two protein molecules that fit together as lock and key promote the abnormal formation of blood vessels in joints affected by rheumatoid arthritis after observing that the substances are present at higher levels in the joints of patients affected by the disease.

One of the study's authors, Shiva Shahrara (University of Illinois), discussed the results, saying: "Our results show, for the first time that these two proteins – a receptor and its corresponding binding protein – play a key role in the progression of rheumatoid arthritis pathology. The swelling of joints is caused by the abnormal migration of a variety of different cell types into the joint and as these cells accumulate, they need to be supplied with oxygen and nutrients, and so angiogenesis accompanies the joint swelling."

Shahrara and her team were aware that a protein called CCL28 was found in the body under low oxygen conditions, or hypoxia. Joints affected by rheumatoid arthritis can become hypoxic, so the researchers wanted to see if the protein and its receptor could be found in patients' affected joints.

In the study the team measured the levels of the proteins in the tissues and fluid of joints from patients with rheumatoid arthritis and with osteoarthritis. Patients of both types had protein levels in their joints that were significantly higher than individuals without joint disease.

The investigators reported that CCL28, which is overproduced in joints affected by rheumatoid arthritis, attracts the surface-lining cells that carry its receptor.

When the researchers added CCL28 to cells carrying the receptor, the cells organized into blood vessels. But if they chemically blocked the receptor and added CCL28, formation of blood vessels was reduced.

The finding, Shahrara said, provides "strong evidence" that the binding of CCL28 to joint-lining cells carrying its corresponding receptor is a necessary step in angiogenesis.

Source: University of Illinois press release: www.eurekalert.org/pub_releases/2014--05/uoia-mii051614.php – All stories written by Dominic Chamberlain

About the News

The News highlights some of the most important events and research in the field of rheumatology. If you have newsworthy information, please contact: Dominic Chamberlain, Commissioning Editor, *International Journal of Clinical Rheumatology*, Future Medicine Ltd, d.chamberlain@futuremedicine.com