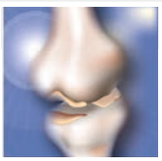
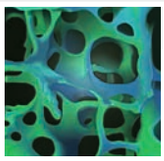


Bulletin Board

T-cell targeted therapy offers relief to psoriatic arthritis patients

It is widely believed that approximately 7.5 million Americans (~2.2% of the population) suffer from psoriasis, an autoimmune disease causing red, flaky skin. A new study recently published in the *Journal of the American Academy of Orthopedic Surgeons* has demonstrated that patients with psoriatic arthritis (PsA), a type of arthritis that affects nearly 48% of patients afflicted with psoriasis, can significantly benefit from medications or biologic agents that target T cells.

"Although these new immunosuppressive agents are expensive, they are the only agents that have demonstrated a decrease in radiologic progression of peripheral arthritis, and can be used to manage associated types of inflammation, as well as skin and nail disease" explains lead author of the study Michael Day, a resident orthopedic surgeon with the Department of Orthopedic Surgery at NYU Hospital for Joint Diseases.

PsA can occur in a wide range of intensities, exhibiting mild symptoms that involve only a few joints, to severe symptoms, affecting a larger number of joints and causing substantial pain. Day outlines that even though skin lesions appear before arthritic symptoms in approximately 15% of patients, those with more severe psoriasis are not necessarily at greater risk for developing PsA.

Susan Goodman, co-study author and assisting attending rheumatologist and internist at the Hospital for Special Surgery (NY, USA) added, "When patients in dermatology clinics are screened for evidence of inflammatory arthritis, many have evidence of joint inflammation that they did not report, suggesting that many of these patients are undiagnosed and untreated."

NSAIDs are currently used as an initial treatment for PsA reducing inflammation, pain and fever. Goodman, however, adds that in the near future, patients will be able to avoid progressing to end-stage arthritis and joint destruction through drugs designed to provide a more targeted therapy.

As PsA and rheumatoid arthritis share many similarities, PsA researchers have been encouraged to consider treating patients earlier and more aggressively, a strategy that has been shown to be successful in rheumatoid arthritis patients.

Patients with joint deformities caused by PsA can also be considered for surgery; however, few large-scale, high-quality clinical trials exist according to Day, adding that, "The disease typically follows a moderate course, but up to 48% of cases develop into destructive arthritis in which the inflammatory process leads to bone erosion and loss of joint architecture."

Although orthopedic surgeons play an important role in the PsA treatment team, the basis for a successful surgery of PSA patients is the collaboration between dermatologists, rheumatologists, internists and family physicians.

Day concludes, "PsA is a systemic inflammatory disease with multiorgan system effects. As such it should be treated with a multidisciplinary approach."

– Written by Paolo Reveglia

Source: Day MS, Nam D, Goodman S, Su EP, Figgie M. Psoriatic arthritis. *J. Am. Acad. Orthop. Surg.* 20(1), 28–37 (2012).

in the news...

Study finds women suffering from systemic lupus erythematosus and rheumatoid arthritis give birth to fewer children

More than half of women who suffer from rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) have fewer children than desired, according to new research published in *Arthritis Care and Research*. The results suggest that higher rates of infertility and miscarriage may also impact the number of offspring born to women with these chronic conditions. However, patient choice in the study is thought to have some influence on the observed smaller family size.

According to the American College of Rheumatology (GA, USA), up to 322,000 and 1.3 million US adults suffer from SLE and RA, respectively. Reports have shown that both RA and SLE are more common in women, especially during reproductive years.

The study was designed to investigate the role of fertility, pregnancy loss and family size choice in women with RA and SLE. A total of 1017 female patients in the National Data Bank for Rheumatic Diseases were surveyed, with respondents to the reproductive health questionnaire including 578 women with RA and 114 with SLE. Based on the responses of the participants, they were divided into the following categories: those interested in having children at symptom onset who had either fewer children than planned (group A); the same number as planned (group B); and those no longer interested in having children at diagnosis (group C).

The results of the study highlighted that over 60% of respondents were in group C, and that 55% of women with RA and 64% with SLE had fewer children then originally planned. In addition, the infertility rate of women with RA in group A was 1.5-times higher than those in group B; however, both groups had similar rates of miscarriage. By contrast, women with SLE in group A had a similar number of pregnancies as those in group B, but a threefold higher miscarriage rate.

Overall, in women diagnosed with RA during childbearing years, the infertility rate was higher than in those diagnosed after childbearing age was complete. No significant increase in infertility was observed in patients with SLE; however, participants with lupus who had fewer children than desired were found to be associated with pregnancy loss.

The authors conclude that patient education to enhance awareness of safe medical options during pregnancy and effective control of these autoimmune diseases will assist women with achieving their childbearing goals.

An author of the study, Megan Clowse, explained, "Our study highlights important reproductive health concerns for women with RA and lupus … Further study of the underlying causes of infertility and pregnancy loss in women with RA and SLE is needed to help fulfill their desire for children."

– Written by Paolo Reveglia

Source: Clowse ME, Chakravarty E, Costenbader KH, Chambers C, Michaud K. The effects of infertility, pregnancy loss, and patient concerns on family size of women with rheumatoid arthritis and systemic lupus erythematosus. *Arthritis Care Res.* doi:10.1002/acr.21593 (2012) (Epub ahead of print).

Prospective study adds to evidence for suggested association between hip fractures and proton pump inhibitor use

Results from a large cohort study published in the *BMJ* have raised doubts over the safety of long-term use of proton pump inhibitors (PPIs) in postmenopausal women after finding a significant association with hip fractures that was linked to duration of use. The US-based cohort of nearly 80,000 patients found a 35% increased risk of hip fracture for those who had used PPIs for over 2 years, an effect that was more substantial in those with a history of smoking. The prospective results add to recent findings of an association on fractures and may lead to more careful use and labeling of the common therapy, especially among menopausal women who smoke.

PPIs are one of the most widely used drugs worldwide and are prescribed 'over the counter' for gastrointestinal conditions, such as heartburn, gastroesophageal reflux and peptic ulcers. Previous studies have suggested an association of the drug with hip fractures, potentially due to their effect on calcium absorption and osteoclast function; however, this study is the first large-scale prospective study to incorporate dietary and lifestyle factors to enable researchers to adjust the results for other risk factors.

Using the Nurses' Health Study cohort of 79,899 postmenopausal women followed from 2000 to 2008, the researchers from Massachusetts General Hospital (MA, USA) recorded hip fracture incidence as well as lifestyle factors, such as

alcohol intake, BMI, smoking and physical activity.

Among regular users of PPIs, the rate of hip fracture was 2.02 events per 1000 person-years, 35% higher when compared with the 1.51 events per 1000 person-years among non-users. This risk increased with longer regular use of PPIs. Adjustment for risk factors, including intake of calcium did not materially alter this association. Those who smoked and used PPIs had a greater than 50% increase in risk of fracture. Interestingly, incorporating smoke history into the analysis implied that the effect between PPI use and hip fractures was confined to women who had smoked, with no significant effect seen in those who had never smoked.

Owing to the association highlighted in this study, the US FDA plans to revise labeling on PPIs. The researchers also called for an increased risk assessment in the needs of women who have previously smoked. Despite the gravity of the implications, the researchers did highlight that following discontinuation of regular PPI use, the risk of hip fracture returned to normal within 2 years.

– Written by Louise Rishton

Source: Khalili H, Huang ES, Jacobson BC, Camargo CA Jr, Feskanich D, Chan AT. Use of proton pump inhibitors and risk of hip fracture in relation to dietary and lifestyle factors: a prospective cohort study. *BMJ* 344, e372 (2012).

Rate of malignancy higher in children with juvenile idiopathic arthritis, study reveals

According to a study published in *Arthritis and Rheumatism*, the incidence of malignancy among children with juvenile idiopathic arthritis (JIA) is four-times higher than in those without the disease. The findings go on to suggest that JIA treatment, such as TNF inhibitors, do not necessarily account for the development of cancer in this pediatric population.

A reported 600,000 people worldwide are thought to have received anti-TNF therapy since its introduction in 1997. Since then, 'black box' warnings highlighting potential malignancy risk have been included by the US FDA on the labels of TNF inhibitors.

The current study was one of the largest investigations into the rates of malignancy among JIA pediatric patients relative to their treatment. Timothy Beukelman from the University of Alabama (AL, USA) and colleagues studied data from the US Medicaid records from the year 2000 through to 2005. In total, 7812 children with JIA were identified along with two comparator groups without JIA: 652,234 children with asthma and 321,821 children with attention-deficit/hyperactivity disorder.

Patients' treatment with methotrexate and TNF inhibitors were categorized as 'ever' or 'never' used. Many children within the JIA group did not receive either of these during the study. In the JIA cohort of 7812 children, a total follow-up time of 12,614 person-years, of whom 1484 children contributed 2922 person-years of anti-TNF exposure. The incidence rate among children with JIA compared to those without was found to be 4.4-times higher for probable and highly probable malignancies. The study additionally found that patients with JIA treated with MTX without TNF inhibitors had a similarly increased incidence of cancer, which was 3.9-times higher than children without JIA.

"While our findings show children with JIA have a higher incidence of cancer compared to peers without JIA, the greater frequency of malignancy does not appear to be necessarily associated with treatment, including use of TNF inhibitors. This highlights the critical importance of appropriate comparator groups when evaluating the safety of new medications. Further confirmation of our findings with large-scale and long-term investigation of the association between cancer and JIA, and its treatment is needed" Beukelman concluded.

– Written by Paolo Reveglia

Source: Beukelman T, Haynes K, Curtis JR *et al.* Rates of malignancy associated with juvenile idiopathic arthritis and its treatment. *Arthritis Rheum.* doi:10.1002/art.34348 (2012) (Epub ahead of print).

Glucocorticoid therapy could potentially decrease protein citrullination in joints of rheumatoid arthritis patients

Recent research published in *Arthritis Research and Therapy* has demonstrated that the levels of citrullination and peptidylarginine deiminase 4 (PAD-4; the enzyme responsible for citrullination) in the joints of rheumatoid arthritis (RA) patients can be reduced through glucocorticoid (GC) therapy.

RA is a chronic inflammatory autoimmune disease and the National Rheumatoid Arthritis Society states that it affects "580,000 people in England, which suggests that over 690,000 adults in the UK live with the condition." The rate of disease progression is different among individuals, and RA can cause serious disability that can have a strong impact on a person's quality of life.

Authors of the research explain that the disease is characterized by the presence of highly specific antibodies, known as anti-citrullination protein antibodies, that identify various different citrullinated proteins (CPs). They explain that

"citrullination is the conversion of peptidylarginine to peptidylcitrulline through a calcium-dependent process catalyzed by the [PAD] enzymes." Only expression of two of the five isotypes of PADs described in humans, namely PAD-2 and -4, have been demonstrated in the inflamed synovial tissue in RA, as well as in other types of inflammatory arthritis disease types.

RA patients have high levels of protein citrullination in the inflamed joints, and it is believed that these proteins play a role in the initiation and maintenance of joint inflammation in RA patients. In the study, scientists examined biopsies taken from 11 RA patients treated with methotrexate, 15 RA patients treated with intra-articular GC injection, eight healthy individuals and five osteoarthritis patients. Scientists analyZed synovial inflammation using a "double-blind semiquantitative analysis of lining thickness, cell infiltration and vascularity using a 4-point scale." Furthermore, among other examinations carried out during the study, scientists also examined the expression of CPs with monoclonal antibody F95, as well as PAD-2 and -4.

Results demonstrated increased levels of CPs in the knees of RA patients when compared to the joints of control patients. Elevated levels of PAD-2 and -4 were discovered in RA-patient biopsies, and scientists found a correlation between the extent of inflammation and CP and PAD levels – inflammation worsened with higher levels of CP and PAD.

Scientists also observed that intra-articular GC treatment decreases both total and intracellular expression of CP, and PAD-4 expression also decreased. Authors write, "In contrast methotrexate treatment had no effect on either synovial inflammation or local expression of CP and PAD."

When investigators tested a synthetic GC known as dexamethasone in synovial fluid and blood from RA patients, a reduction in CP and PAD-2 or -4 was observed only in cells from the synovial fluid.

Increased knowledge of RA will help develop future treatments for the condition and will also contribute towards improved management of the disease. Anca Catrina (Karolinska University Hospital, Karolinska Institutet, Sweden), states, "Our work has been able to establish for the first time that different treatments have different effects on protein citrullination, an important process in the progression of RA."

– Written by Roshaine Gunawardana

Sources: Makrygiannakis D, Revu S, Engstrom M *et al.* Local administration of glucocorticoids decrease synovial citrullination in rheumatoid arthritis. *Arthritis Res. Ther.* 14(1), R20 (2012); National Rheumatoid Arthritis Society: www.nras.org.uk

in brief...

The public health impact of risk factors for physical inactivity in adults with rheumatoid arthritis. Lee J, Dunlop D, Ehrlich-Jones L *et al. Arthritis Care Res.* doi:10.1002/acr.21582 (2012) (Epub ahead of print).

Results of a new study suggest that over two in five adults (42%) who suffer from rheumatoid arthritis may be physically inactive. Two factors were related to almost 65% inactivity in this sample; lack of strong motivation and lack of strong beliefs related to physical activity. The results indicate that public initiatives should be developed to increase motivation for physical exercise and that lead to stronger beliefs towards the benefits of physical exercise.

About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of rheumatology. If you have newsworthy information, please contact:

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