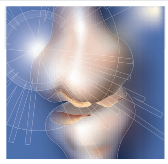
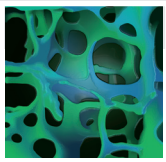


Bulletin Board

Tocilizumab found to be effective replacement for anti-TNF therapy in rheumatoid arthritis

Tocilizumab has been shown to be effective, in concert with methotrexate, in rheumatoid arthritis patients who do not respond to anti-tumor necrosis factor (TNF) therapy, according to a new study. Tocilizumab is a monoclonal antibody that blocks the interleukin (IL)-6 receptor.

"This is the first study looking at the impact of blocking the effects of interleukin-6 in patients who have failed TNF antagonist therapy," commented Paul Emery (University of Leeds, UK), lead author of the study. "The 'take-home' message is that IL-6 blockade offers a realistic alternative for (these) patients."

In this Phase III trial, 499 individuals with rheumatoid arthritis were randomized to receive either 4 or 8 mg/kg tocilizumab or placebo, intravenously every 4 weeks for a total of 24 weeks. All the patients had not responded well to one or more anti-TNF drugs, and they were all also given methotrexate during the 24-week period.

At the end of the 24-week period, 50% and 30.4% of patients who had been given 8 mg/kg or 4 mg/kg of tocilizumab, respectively, had an American College of Rheumatology (ACR)20 response; the latter is a measure of therapeutic efficacy. By contrast, only 10.1% of the patients in the control group achieved an ACR20 response at 24 weeks. The results were statistically significant.

Tocilizumab was found to be efficacious regardless of the most recently failed anti-TNF agent or the number of failed treatments. "The finding of equal efficacy after one or two TNF antagonist failures was unusual," Emery stated.

The disease remission rates at week 24 were related to the dose; 30.1% and 7.6% of the patients in the 8 mg/kg and 4 mg/kg tocilizumab groups, respectively, achieved remission, compared with only 1.6% of the patients in the control group.

Approximately 85% of patients in each tocilizumab group and 81% in the control group had an adverse event, but in almost all cases the side effect was mild or moderate and could be managed easily. The most common adverse events with a higher incidence in the tocilizumab group were infections, gastrointestinal symptoms, rash and headache. Serious events were found to be more common in the control, placebo group than the tocilizumab group.

"Tocilizumab plus methotrexate is effective in achieving rapid and sustained improvements in signs and symptoms of RA in patients with inadequate response to TNF antagonists, and has a manageable safety profile," concluded Emery.

"Once tocilizumab becomes licensed in other countries, as it is currently in Japan, we will have further expanded the therapeutic options that in turn will allow an increase in the proportion of rheumatoid arthritis patients who achieve a good clinical outcome," Josef S Smolen and Michael E Weinblatt wrote in an accompanying editorial.

Source: Emery P, Keystone E, Tony HP *et al.*: IL-6 receptor inhibition with tocilizumab improves treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumour necrosis factor biologicals: results from a 24-week multicentre randomised placebo-controlled trial. *Ann. Rheum. Dis.* 67(11), 1516–1523 (2008); Smolen JS, Weinblatt ME: When patients with rheumatoid arthritis fail tumour necrosis factor inhibitors: what is the next step? *Ann. Rheum. Dis.* 67(11), 1497–1498 (2008).

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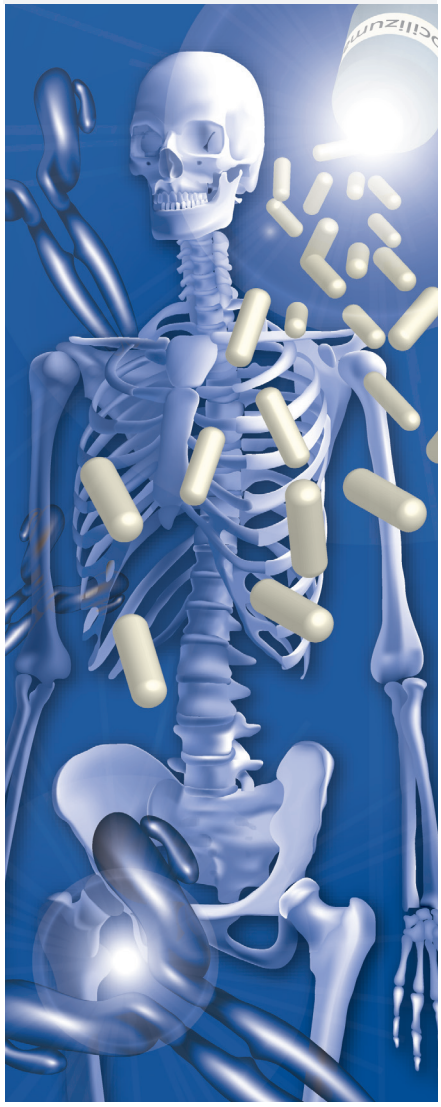

Psoriatic arthritis treatment guidelines developed

The first international guidelines for the treatment of psoriatic arthritis (PsA) have been published recently by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), whose members include rheumatologists, dermatologists and PsA patients. The disorder usually manifests in individuals who already suffer from psoriasis, but occasionally the arthritis develops first.

> "These guidelines are designed as a platform to make sure physicians around the world are aware of what's available for their patients and to help them make sound treatment decisions."

"In the past few years, new medications have become available that are incredibly effective for the various manifestations of psoriatic arthritis," explained Christopher Ritchlin, lead author. "Many patients' find their lives changed for the better within just a couple of weeks. These guidelines are designed as a platform to make sure physicians around the world are aware of what's available for their patients and to help them make sound treatment decisions."

"The presenting symptoms of psoriatic arthritis vary tremendously from patient to patient," commented Ritchlin. "It's a very challenging disease to treat, because so many different parts of the body can be involved. Oftentimes a patient will come in with something you might call 'tennis elbow,' or they might have a sore Achilles heel, and that's their only symptom. It can be very difficult to diagnose."

Physicians have a number of options for the treatment of PsA, including injecting NSAIDs like ibuprofen into affected joints or tendons. Another commonly used option is a disease-modifying anti-rheumatic drug, like methotrexate; however, GRAPPA found that they were not as effective for PsA as they are for rheumatoid arthritis.

At present, there are a large number of PsA patients who have never consulted a rheumatologist and many who are undiagnosed; therefore, the group stressed the importance of consulting a specialist as soon as psoriasis or PsA is suspected.

One further recommendation was that physicians should consider newer medications, anti-TNF drugs, in the treatment of PsA. The US FDA approved the use of etanercept, the first anti-TNF drug, for rheumatoid arthritis in 1998; it was subsequently approved for PsA in 2002. Currently, fewer than 20% of PsA patients are receiving anti-TNF drugs.

Sources: Ritchlin CT, Kavanaugh A, Gladman DD *et al.*: Treatment recommendations for psoriatic arthritis. *Ann. Rheum. Dis.* (Epub ahead of print) (2008); *ScienceDaily*: www.sciencedaily.com /releases/2008/10/081026150155.htm

About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of rheumatology.

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Priority Paper Alerts

Self-reported osteoarthritis, ethnicity, body mass index, and other associated risk factors in postmenopausal women – results from the Women's Health Initiative.

Wright NC, Riggs GK, Lisse JR, Chen Z: *J. Am. Geriatr. Soc.* (Epub ahead of print) (2008).

The aim of this study was to ascertain risk factors for self-reported osteoarthritis in an ethnically diverse group of women, consisting of 146,494 postmenopausal women between the ages of 50 and 79, who are participants of the clinical trial and observational study of the WHI. The risk factors that contributed most strongly to self-reported osteoarthritis were found to be older age and higher BMI. Obesity was most prevalent in African–Americans (57.9%), followed by American–Indians (51%), Hispanic whites (41.9%) and non-Hispanic whites (32.9%). The odds of self-reported osteoarthritis were higher for American–Indian and African–American women, which suggested that BMI and ethnicity interact to affect the odds of OA. The authors concluded that osteoarthritis is very common in postmenopausal women and that ethnicity plays a role.

Perinatal characteristics, early life infections, and later risk of rheumatoid arthritis and juvenile idiopathic arthritis.

Carlens C, Jacobsson LT, Brandt L, Cnattingius S, Stephansson O, Askling J. *Ann. Rheum. Dis.* (Epub ahead of print) (2008).

The objective of this nationwide register-based case-control study was to investigate the effect of birth features and early life infections on the risk of developing rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) in later life. The researchers used the Swedish Inpatient Register and the Early Arthritis Register to identify cases and the Swedish Medical Birth Register to select 4 matched controls per case. They found a link between infections during first year of life and a higher risk for developing sero-negative RA. The authors concluded that infections during the first year of life could play a role in the etiology of adult RA and JIA.

Conventional bone builders used to treat steroid-induced bone loss

A novel study presented at the American College of Rheumatology (ACR)–Association of Rheumatology Health Professionals (ARHP) Annual Scientific Meeting suggests that drugs used in the treatment of osteoporosis can also be used to treat glucocorticoid-induced osteoporosis.

The aim of the multicenter trial, carried out by Kenneth Saag, from the University of Alabama at Birmingham, AL, USA, and colleagues, was to compare the efficacy of teriparatide and alendronate in individuals with glucocorticoid-induced osteoporosis. Alendronate is a bisphosphonate used in the prevention and treatment of osteoporosis. Teriparatide is a third-line agent (following calcium/vitamin D supplementation and bisphosphonates), and it is a drug based on the parathyroid hormone. The drug has been shown to stimulate bone formation.

In the trial, patients who had taken glucocorticoids for 3 months or longer were randomly assigned to receive either teriparatide 20 µg/day (214 patients) or alendronate 10 mg/day (214 patients), and were followed for up to 3 years, making it the longest clinical trial with teriparatide. The researchers used dual-energy x-ray absorptiometry to measure bone mineral density (BMD).

> "The bulk of patients are not receiving testing or treatment for osteoporosis when they are on chronic steroid therapy."

Increases in BMD at the lumbar spine and femoral neck, which are common fracture sites in individuals taking glucocorticoids, were found to be greater in patients receiving teriparatide compared with those who were given alendronate. The results were statistically significant for both locations at 36 months.

In addition, only 3 out of the 173 patients in the teriparatide group had new radiographic vertebral fractures, compared with 13 out of the 169 that belonged to the alendronate group (1.7 versus 7.7%; p = 0.007). There was no significant difference between the two groups as far as new nonvertebral fractures were concerned.

"The study showed significant risk reduction in incident vertebral fractures in the studied patients," stated Saag.

"The bulk of patients are not receiving testing or treatment for osteoporosis when they are on chronic steroid therapy," concluded Saag. "The data suggest therapies that should be considered for high-risk patients on glucocorticoids."

Source: Saag KG, Zanchetta JR, Devogelaer JP *et al.*: Teriparatide versus alendronate for treatment of glucocorticoid-induced osteoporosis: 36-month results. Abstract 2101. Presented at: *The ACR-ARHP Annual Scientific Meeting*, October 24–29, 2008.

Risk of cancer not increased through use of anti-TNF therapies for rheumatoid arthritis

A new study, presented at the ACR–ARHP Annual Scientific Meeting, suggests that there is no association between the use of TNF antagonists for rheumatoid arthritis and an increased risk for developing cancer. The research showed that the incidence of cancer in a group of individuals treated with anti-TNF drugs was similar to a control group.

The researchers from the Spanish Foundation of Rheumatology in Madrid utilized a national drug registry called BIOBADASER in order to investigate a possible association between anti-TNF therapy and the incidence of cancer. The registry was established in 2001 to carry out long-term follow-up on the safety of biological treatments in rheumatoid arthritis. The registry contains information on 4529 rheumatoid patients treated with anti-TNF drugs, including details such as gender, diagnosis date, treatment information and any adverse reactions that the patient may have experienced. For the control group, they used an external cohort consisting of 789 rheumatoid arthritis patients who were not given anti-TNF drugs.

> "Despite foreseen fears, blocking the tumor necrosis factor does not make patients more prone to develop cancer."

In total, 70 incidences of cancer were recorded in the anti-TNF group and 29 in the control cohort, but after adjusting for factors such as gender and age, amongst others, a 0.92 incidence of cancer was observed in the control group, a figure similar to the anti-TNF patients. These results led the authors to conclude that TNF use did not confer an increased risk for developing cancer.

"Despite foreseen fears, blocking the tumor necrosis factor does not make patients more prone to develop cancer. All on the contrary, blocking the inflammation cascade may help diminish the overall risk of cancer in these patients," concluded Loreto Carmona, lead author of the study.

Source: Abásolo L, Carmona L, Gómez-Reino JJ: Is the exposure to TNF antagonists a risk factor for cancer in rheumatoid arthritis? Abstract 1266. Presented at: *The ACR-ARHP Annual Scientific Meeting*, October 24–29, 2008.