

New Tool Will Calculate Absolute Fracture Risk

BY SHERRY BOSCHERT
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SAN FRANCISCO — A yet to be released tool developed by the World Health Organization should help physicians calculate an individual's absolute risk for bone fracture and provide a basis for counseling patients regarding treatment, experts said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

The expected WHO model will estimate an individual's risk of developing a fragility fracture over the next decade, based on factors that may include age, bone mineral density of the femoral neck, a history of previous fracture, family history of fracture, smoking and alcohol use, steroid use, and the presence of rheumatoid arthritis.

At this point no one knows exactly which factors will be included in the model, said Steven T. Harris, M.D., clinical pro-

fessor of medicine at the University of California, San Francisco.

Calculating absolute risk for fracture greatly assists therapeutic decision-making, he said. For example, a 2001 model looked at the 10-year probability of fractures in the hip, forearm, humerus, or spine based simply on age and bone density. A 45-year-old with a T score of -3 (which is consistent with osteoporosis) has about a 10% risk of fracture over the next 10 years, but the fracture risk in-

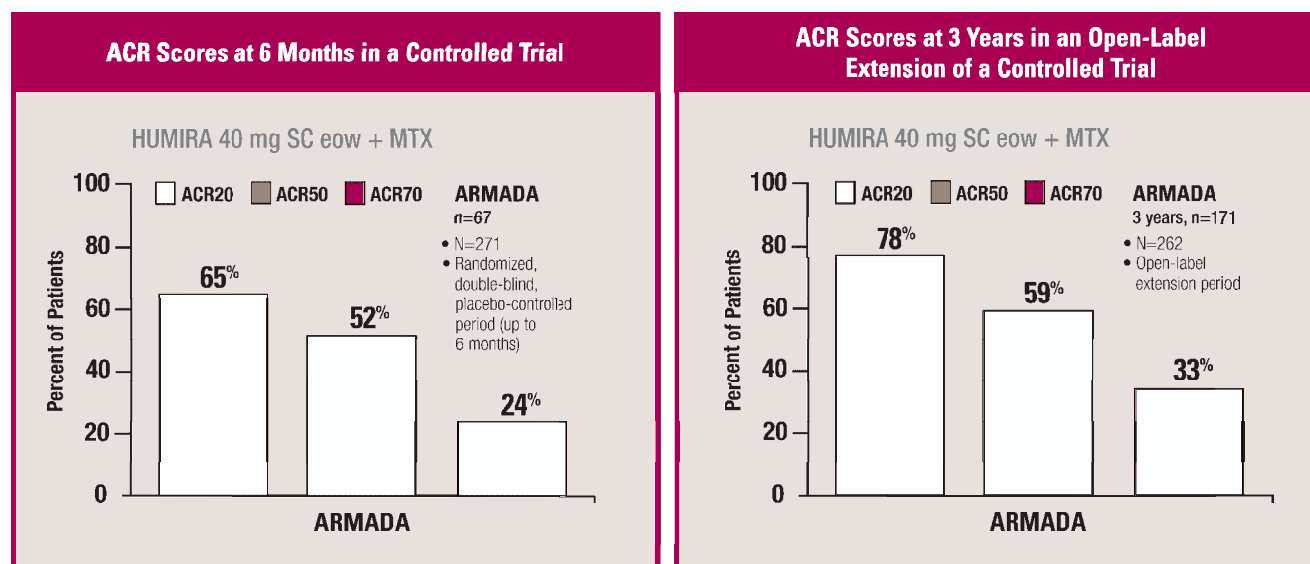
creases to 30% in a 75-year-old with the same bone density.

The WHO model "is going to be far better than telling someone they have osteoporosis, giving them a prescription, and saying goodbye," Dr. Harris said. "Getting people engaged in conversation about what their risk is, and what can be done with contemporary treatment, is going to make therapy a lot more rational."

If a clinician could tell a 55-year-old patient who is osteopenic (with a T score of

IT'S ABOUT RESPONSE

ACR SCORES MAINTAINED IN MODERATE-TO-SEVERE RA²⁻⁴



The above analysis is the intent-to-treat study population using nonresponder imputation methodology. Patients who withdrew or had missing values were considered nonresponders.

The above analysis is as-observed at the indicated time points. Patients with missing data were excluded.

TRIALS DESIGNED TO MATCH REAL-LIFE PATIENTS^{1,3-6}

BASELINE PATIENT DEMOGRAPHICS IN HUMIRA TRIALS ARMADA + DE019^{1,3-6}

- All trial patients had inadequate response to MTX
- Failed up to 3 DMARDs
- Disease duration (years): 10.0 to 12.5
- Mean HAQ DI: 1.4 to 1.6
- Mean CRP (mg/dL): 1.6 to 3.1

IMPORTANT SAFETY INFORMATION

HUMIRA is indicated for reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDs. HUMIRA can be used alone or in combination with MTX or other DMARDs.

TUBERCULOSIS (TB) AND INVASIVE OPPORTUNISTIC FUNGAL INFECTIONS HAVE BEEN OBSERVED IN PATIENTS TREATED WITH TNF-BLOCKING AGENTS, INCLUDING HUMIRA. PATIENTS SHOULD BE EVALUATED FOR LATENT (INACTIVE) TB WITH A SKIN TEST. TREATMENT OF TB SHOULD BE INITIATED PRIOR TO THERAPY WITH HUMIRA. THE BENEFITS AND RISKS OF HUMIRA SHOULD BE CAREFULLY CONSIDERED BEFORE INITIATION OF TREATMENT FOR PATIENTS WHO HAVE RESIDED IN REGIONS WHERE TB OR HISTOPLASMOSIS IS ENDEMIC.

SERIOUS INFECTIONS AND SEPSIS, INCLUDING FATALITIES, HAVE BEEN REPORTED WITH THE USE OF TNF-BLOCKING AGENTS, INCLUDING HUMIRA. MANY OF THESE INFECTIONS OCCURRED IN PATIENTS PREDISPOSED TO INFECTIONS BECAUSE OF CONCOMITANT IMMUNOSUPPRESSIVE THERAPY IN ADDITION TO THEIR UNDERLYING DISEASE. PATIENTS WHO DEVELOP A NEW INFECTION WHILE USING HUMIRA SHOULD BE MONITORED CLOSELY. TREATMENT SHOULD BE DISCONTINUED IF A PATIENT DEVELOPS A SERIOUS INFECTION. DO NOT START HUMIRA IN PATIENTS WITH ACTIVE

INFECTION (INCLUDING CHRONIC OR LOCALIZED), OR ALLERGY TO HUMIRA OR ITS COMPONENTS. EXERCISE CAUTION IN PATIENTS WITH A HISTORY OF RECURRENT INFECTION OR WITH UNDERLYING CONDITIONS, WHICH MAY PREDISPOSE PATIENTS TO INFECTIONS.

The combination of HUMIRA and anakinra is not recommended. TNF blocking agents, including HUMIRA, have been associated in rare cases with exacerbation of demyelinating disease. Exercise caution when considering HUMIRA for patients with these disorders. Lymphoma has been observed in patients treated with TNF-blocking agents. The role of TNF-blocking agents in the development of malignancy is not known.

Anaphylaxis has been reported rarely following HUMIRA administration. Rare reports of pancytopenia including aplastic anemia have been reported with TNF-blocking agents. Medically significant cytopenia (e.g. thrombocytopenia, leukopenia) has been infrequently reported with HUMIRA. The causal relationship of these reports to HUMIRA remains unclear. Worsening congestive heart failure (CHF) has been observed with TNF-blocking agents, including HUMIRA, and new onset CHF has been reported with TNF-blocking agents.

Most frequent adverse events vs placebo from placebo-controlled studies were injection site reactions (20% vs 14%), upper respiratory infection (17% vs 13%), injection site pain (12% vs 12%), headache (12% vs 8%), rash (12% vs 6%), and sinusitis (11% vs 9%). Discontinuations due to adverse events were 7% for HUMIRA vs 4% for placebo.

–2) that the patient's absolute risk for fracture is 10% over the next 10 years, and that contemporary treatments could reduce that risk to 5%, that should help the patient decide whether the potential improvement is worth the cost or inconvenience associated with therapy.

Calculations of absolute risk also are likely to be used by insurers in the near future to decide whether to cover medical therapy for improving bone density. It may be that therapy for someone with a 20% risk of fracture will be covered, but patients with a 10% risk will have to pay for the medications themselves.

The new WHO index is due to be re-

leased "imminently," which probably means in the first half of 2006, Steven R. Cummings, M.D., said in a separate presentation at the meeting.

He noted that the WHO's fracture risk index is based on data from about 60,000 women in 12 cohorts of patients, mostly Europeans, and needs to be validated in other populations, including that of the United States.

Some studies have been using the index

to compare the value of bone density measurements with the value of other risk factors in predicting future fractures. Using the index alone without measuring bone density seems to be pretty good at predicting hip fractures, and is modestly valuable in predicting other types of osteoporotic fractures.

Having "an index of risk factors may be useful, particularly in places where you don't have bone density testing, or if you're

deciding whether or not" to measure a patient's bone density, said Dr. Cummings, professor emeritus of epidemiology and biostatistics at the university and director of clinical research at the California Pacific Medical Center Research Institute.

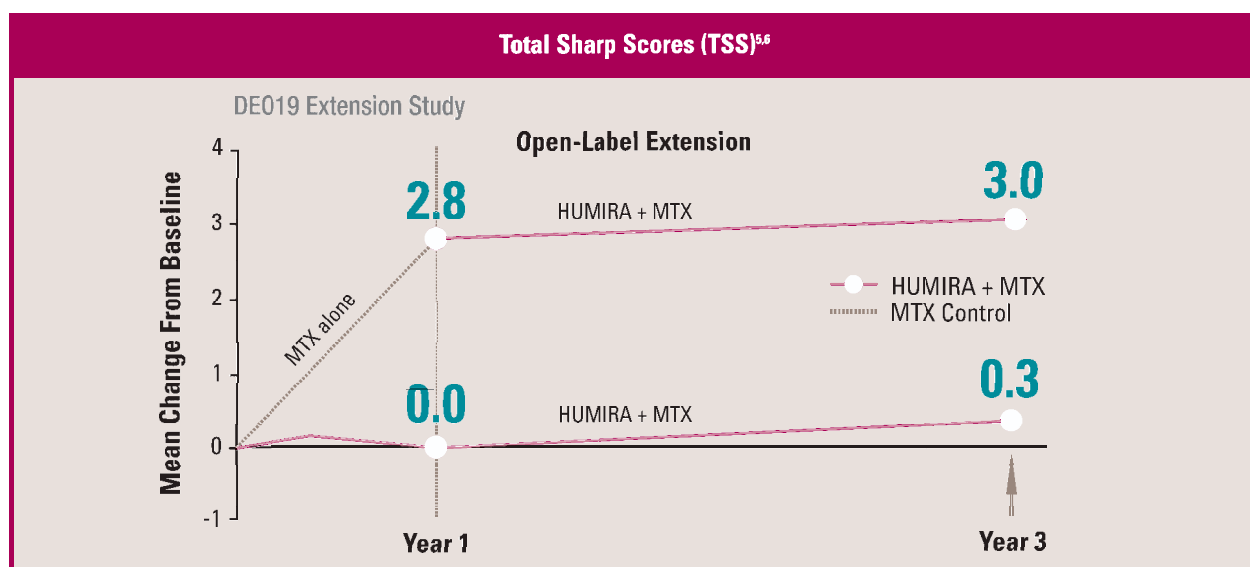
Adding bone density measurement to other factors in the index strengthens the ability to predict hip fracture and mildly strengthens the ability to predict other fractures, but the opposite does not seem to be true. "It's not clear that adding risk factors, once you know the bone density, will substantially improve the clinical judgments you can make about treatment with medication," he said. ■

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IT'S ABOUT

RADIOGRAPHIC EVIDENCE

INHIBITION OF DISEASE PROGRESSION IN MODERATE-TO-SEVERE RA^{5,6}



Year 1 and year 3 x-rays were assessed for changes from baseline in TSS.

Study DE019-619 patients entered a randomized, double-blind, placebo-controlled period up to 1 year. 457 patients entered the open-label extension period.

- In the DE019 extension study, a majority of patients continued to show *no radiographic progression* (≤ 0.5 -unit increase from baseline) at 3 years ($n=129$)⁶
 - 61% based on Total Sharp score (mean change=0.3)
 - 71% based on Joint Erosion score (mean change=0.1)
 - 73% based on Joint Space Narrowing score (mean change=0.2)

HUMIRA[®]
(adalimumab)

References: 1. Data on File. Abbott Laboratories. 2. HUMIRA full prescribing information. 3. Weinblatt ME, Keystone EC, Furst DE, et al. The ARMADA trial: sustained efficacy and long-term safety of adalimumab (HUMIRA[®]) plus methotrexate over 3 years in patients with long-standing rheumatoid arthritis. Presented at: European League Against Rheumatism Annual Scientific Meeting; June 2004; Berlin, Germany. 4. Weinblatt ME, Keystone EC, Furst DE, et al. Adalimumab, a fully human anti-tumor necrosis factor α monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate. *Arthritis Rheum.* 2003;48:35-45. 5. Keystone EC, Kavanaugh AF, Sharp JT, et al. Radiographic, clinical, and functional outcomes

of treatment with adalimumab (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy. *Arthritis Rheum.* 2004;50:1400-1411. 6. Keystone EC, Kavanaugh AF, Sharp JT, et al. Radiographic inhibition of structural damage sustained in patients with long-standing rheumatoid arthritis following 3 years of treatment with adalimumab (HUMIRA[®]) plus methotrexate. Presented at: American College of Rheumatology Annual Scientific Meeting; October 2004; San Antonio, Tex.

Please see brief summary of prescribing information on adjacent page.