Pediatric Use

Safety and efficacy of HUMIRA in pediatric patients for uses other than juvenile idiopathic arthritis have not been established.

Juvenile Idiopathic Arthritis

In the juvenile idiopathic arthritis study, HUMIRA was shown to reduce signs and symptoms of active polyarticular juvenile idiopathic arthritis in patients 4 to 17 years of age. HUMIRA has not been studied in children less than 4 years of age, and there are limited data on HUMIRA treatment in children with weight <15 kg.

Safety of HUMIRA in pediatric patients was generally similar to that observed in adults with certain exceptions *[see Adverse Reactions]*.

Geriatric Use

A total of 519 rheumatoid arthritis patients 65 years of age and older, including 107 patients 75 years of age and older, received HUMIRA in clinical studies RA-I through IV. No overall difference in effectiveness was observed between these subjects and younger subjects. The frequency of serious infection and malignancy among HUMIRA treated subjects over 65 years of age was higher than for those under 65 years of age. Because there is a higher incidence of infections and malignancies in the elderly population in general, caution should be used when treating the elderly.

OVERDOSAGE

Doses up to 10 mg/kg have been administered to patients in clinical trials without evidence of dose-limiting toxicities. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

PATIENT COUNSELING INFORMATION

Patient Counseling

Patients should be advised of the potential benefits and risks of HUMIRA. Physicians should instruct their patients to read the Medication Guide before starting HUMIRA therapy and to reread each time the prescription is renewed.

- **Immunosuppression**

  Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct the patient of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis and reactivation of hepatitis B virus infections.

- **Allergic Reactions**

  Patients should be advised to seek immediate medical attention if they experience any symptoms of severe allergic reactions. Advise latex-sensitive patients that the needle cap of the prefilled syringe contains latex.

- **Other Medical Conditions**

  Advise patients to report any signs of new or worsening medical conditions such as heart disease, neurological disease, or autoimmune disorders. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

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Bisphosphonates Tied to High Jaw Necrosis Risk

BY ALICIA AULT
Associate Editor, Practice Trends

SAN FRANCISCO — The prevalence of osteonecrosis of the jaw appears to be about 1 in 1,700 for adults taking long-term oral bisphosphonate therapy, according to an initial analysis of a group of Kaiser Permanente Northern California members.

Dr. Joan Lo surveyed 13,946 members who'd been taking oral bisphosphonates for at least 1 year and had no known exposure to intravenous bisphosphonate. The researchers received 8,568 responses to the mailed survey, which included questions about dental symptoms, said Dr. Lo, an endocrinologist at the Kaiser Permanente Division of Research, at the annual meeting of the Endocrine Society. Respondents who reported a diagnosis of osteonecrosis, or who reported exposed bone, periodontal disease, delayed bone healing, complications after invasive dental procedures, or persistent symptoms of concern were offered a dental exam by dentists on the PROBE study team. Cases of suspected osteonecrosis of the jaw (ONJ)—defined as exposed bone for greater than 8 weeks in the maxillofacial region, absent prior radiation—were referred for further examination by an oral surgeon. Dental records were reviewed in cases where patients declined a dental exam. Pharmacy records were also reviewed for all patients.

Of those who responded, about 6,402 patients did not have any symptoms of concern. A little more than 2,000 had symptoms of concern; 1,000 of those patients were examined by a dentist.

Dr. Lo said the team had identified eight cases of ONJ so far, for a prevalence of 0.09%, or 1 in 1,100. Three were localized to the palatal torus, and one in the mandible. The remaining four had bone exposure in the mandible following extraction. The confirmed cases had variable areas of bone exposure, variable locations, and various predisposing factors, she said.

In addition, the researchers identified an additional nine patients who had ONJ-like features but did not meet the classic definition of bisphosphonate-related ONJ. Three patients had signs of osteomyelitis of the mandible; an additional four had transient exposure, and another had a small area of bone exposure that persisted up to 1 year but eventually healed after a tooth extraction. The ninth patient had spontaneous tooth loss. Five had evidence of radiographic abnormalities, said Dr. Lo.

With these additional ONJ-like cases, the prevalence increased to 0.2%. Extrapolated to the entire cohort of patients taking bisphosphonates, the prevalence was 1 in 1,729, said Dr. Lo.

The current definition of bisphosphonate-related ONJ may not cover the spectrum of jaw complications seen in patients with long-term exposure, and may underestimate ONJ's prevalence, said Dr. Lo.

Such complications include nonhealing extraction sites and osteomyelitis or osteoporosis without exposed bone. The Kaiser researchers will continue to compile dental records to come up with a more accurate estimate of prevalence, she said.

Dr. Lo disclosed no conflicts of interest related to the study. ■

Bone Erosion and Low Bone Mass May Be Linked in PsA

ELIZABETH MECHCATIE
Senior Writer

A significant association between low bone mass and the presence of bone erosions in patients with psoriatic arthritis suggests there is a relationship between the two in these patients.

Though osteoclasts play a role in both, the relationship between erosions and bone mass in PsA is poorly understood.

Dr. Allen Anandarajah, of the allergy, immunology, and rheumatology unit at the University of Rochester, New York, evaluated data on 1,456 patients with the disease from the Consortium of Rheumatology Researchers of North America (CORRONA) database. "We found the people who had erosions were more likely to have low bone mass," compared with those who don't have erosions, Dr. Anandarajah said at the annual European Congress of Rheumatology.

The study looked at the association between T scores at the lumbar spine and the presence or absence of erosions, adjusting for steroid use, gender, methotrexate use, other disease-modifying antirheumatic drug use, and the use of biologics, as well as for weight, age, body mass index, and disease index.

Of the patients, 567 (40%) had erosions and 889 (60%) had no erosions. The mean age of patients with erosions was 42 years, significantly younger than the patients with none, whose mean age was 45. Significantly more men (51.5%) had erosions than did women (48.5%).

The association between the presence of bone erosions and lower T scores of the lumbar spine was significant, with significantly lower T scores of the lumbar spine among patients with erosions, compared with those who had no erosions. (Focal erosions could be anywhere, he said, noting that the patients in the database usually had x-rays of the hands and feet. But the database includes information on any x-ray that revealed an erosion.)

"These patients do have low bone mass and . . . the mechanism between erosions and generalized bone loss or osteoporosis could be a common factor," Dr. Anandarajah said. ■