**Ocrelizumab Looks Safe, Effective in Phase I/II**

**BY NANCY WALSH**

New York Bureau

**Boston** — A single course of the humanized anti-CD20 antibody ocrelizumab was safe and effective for rheumatoid arthritis (RA) patients who had an inadequate response to methotrexate through 72 weeks. There was no treatment with corticosteroids before the infusions, and patients remained on a stable 10- to 25-mg/week dose of methotrexate through 72 weeks.

Clinical assessments were done every 4 weeks until week 24, at which time efficacy was evaluated, and every 12 weeks thereafter. Most patients were women in their 50s, all of whom had a rheumatoid factor positive, and their mean disease duration exceeded 10 years. Patients had moderate to severe RA and had failed on average at least two disease-modifying drugs. Slightly fewer than half had tried and failed with a tumor necrosis factor receptor blocker, said Dr. Genovese, a rheumatologist at Stanford (Calif.) University.

Rapid depletion of B cells was seen in patients in all active treatment groups after 4 weeks, followed by a gradual dose-dependent rebound. Higher doses demonstrated the greatest efficacy at week 24, with ACR50 responses seen among 25%, 20%, and 18% of patients in the 10-, 50-, and 200-mg groups, respectively. Among placebo patients, ACR50 responses and remission were achieved by 7% and 2%, respectively.

The higher doses also showed greater reductions in C-reactive protein and low immunoglobulin M, he said.

The most frequent adverse events were infusion-related, including headaches, nausea, chills, pyrexia, and dizziness. These events were similar across the active treatment groups and occurred more frequently than in the placebo group.

Rates of serious adverse events were similar across all groups, with 15 events being seen in the placebo group and 14, 20, 23, and 15 events in the 10-, 50-, 200-, and 1,000-mg groups, respectively.

There was one metastatic ovarian cancer in the placebo group, two basal cell carcinomas in the 200-mg group, and one breast cancer in the 50-mg group. No malignancies were seen in the highest dose group.

Administration of ocrelizumab was tied to a slight decrease in immunoglobulin M levels, but this did not appear to have any clinical significance, since there were no infections associated with this decrease, he said. Dr. Genovese disclosed financial ties to tri-funder Genentech Inc. as well as Biogen Idec Inc., and Hoffmann-LaRoche Ltd.

**Meniscal Damage Predicts Likelihood of Radiographic Knee OA**

**BY DIANA MAHONEY**

New England Bureau

**Boston** — Preventing meniscal damage should be a top therapeutic priority in the fight against knee osteoarthritis, Dr. Martin Englund said at the annual meeting of the American College of Rheumatology.

The Multicenter Osteoarthritis study (MOST) demonstrated for the first time that meniscal damage without surgical resection is a risk factor for radiographic knee osteoarthritis.

The onset of knee osteoarthritis (OA) after the surgical removal of all or part of a torn meniscus is common, and numerous longitudinal studies have identified meniscectomy as a significant risk factor for knee OA, according to Dr. Englund, of Boston University, and his colleagues. However, no studies have demonstrated that meniscal damage without surgical resection is associated with the development of incident radiographic knee OA (ROA), he said. To evaluate the effect of baseline meniscal damage on incident Tibiofemoral radiographic OA, the researchers conducted a nested case-control investigation comprising patients enrolled in the MOST study, a prospective observational study of 3,026 individuals older than age 50 who have or are at high risk for knee OA.

Prior knee surgery patients were excluded. Participants had standardized, weight-bearing, fixed-flexion x-rays at baseline and at 30 months.

Meniscal damage at baseline was 52% more common in case knees versus 18% of controls.

**DR. ENGLUND**

These x-rays were read paired by a musculoskeletal radiologist and rheumatologist, both blinded to clinical and MRI data, Dr. Englund explained. For the current study, 52 knees with no Tibiofemoral ROA at baseline but evidence of grade 2 or higher ROA on the Kellgren-Lawrence scale in the 30-month follow-up were cases; 130 knees drawn from the same source population but with no Tibiofemoral ROA at follow-up were controls.

To assess the baseline meniscal status of the knees, two blinded musculoskeletal radiologists reviewed coronal and sagittal fast spin echo MRI images and evaluated each on a collapsed scale. Knees with no meniscal damage were grade 0, those with a minor tear were grade 1, and those with a nondisplaced tear, displaced tear, maceration, or destruction were considered grade 2.

The investigators analyzed the link between meniscal damage and ROA using two logistic regression models (one in which the meniscal score was entered as 0, 1, or 2, and one in which it was entered as meniscal damage or no damage) adjusted for age, sex, body mass index, physical activity, and mechanical knee alignment.

“Meniscal damage at baseline was significantly more common in cases than in controls,” Dr. Englund reported, evident in 52% of case knees, versus 18% of controls. In a multivariable model, the odds ratio of incident Tibiofemoral ROA increased as the meniscal score increased, Dr. Englund noted. When knees with meniscal damage were compared with knees that had a normal meniscus at baseline, the adjusted odds ratio for ROA at 30 months was 4.3 for knees with a meniscal score of 1 and 7.8 for those with a meniscal score of 2.

Dr. Englund disclosed no financial conflicts related to his presentation.