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 in a phase I/II trial, Dr. Mark Genovese reported at the annual meeting of the American College of Rheumatology.

Ocrelizumab is similar to the chimeric anti-CD20 antibody rituximab in its ability to deplete B cells, but this second-generation antibody differs in its Fc region by two amino acid sequences, resulting in slightly increased antibody-dependent cytotoxicity and slightly decreased complement-dependent toxicity, Dr. Genovese said.

The trial included 237 rheumatoid arthritis (RA) patients who had an inadequate response to methotrexate and received a single course of ocrelizumab in doses of 10 mg, 50 mg, 200 mg, 500 mg, or 1000 mg or placebo, given by intravenous infusion on days 1 and 15. 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 were rheumatoid factor positive, and their mean disease duration exceeded 10 years. At baseline, 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 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 the infusions, followed by a gradual dose-dependent repletion. Higher doses demonstrated the greatest efficacy at week 24, with ACR50 responses seen among 25%, 20%, and 28% of patients in the 200-, 500-, and 1,000-mg groups. Remission was achieved by 10%, 3%, and 8% of patients in these 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 immunogenicity, 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, 18, 23, and 15 events in the 10-, 50-, 200-, 500-, and 1,000-mg groups, respectively.

There was one metastatic ovarian cancer in the placebo group, two basal cell carcinomas in a single patient at the 10-mg dose, one laryngeal cancer and one breast cancer in the 50-mg group, one B-cell lymphoma in the 200-mg group, and one adenocarcinoma and two basal cell carcinomas in the 500-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 trial funder Genentech Inc. as well as Biogen Idec Inc., and Hoffmann-LaRoche Ltd. ■

New DEA Rule Allows Multiple Prescriptions for Pain Drugs

BY ALICIA AULT
Associate Editor, Practice Trends

In a reversal, the Drug Enforcement Administration will now allow physicians to write up to three prescriptions for a 90-day supply of schedule II controlled substances.

The final rule, published in November, is viewed as a victory by pain medicine specialists, said Dr. B. Todd Sitzman, American Academy of Pain Medicine president and director of advanced pain therapy at the Forrest General Hospital's cancer center in Hattiesburg, Miss.

"It's an indication that [DEA officials] have listened to pain physicians and to the pain patient community," he said in an interview.

The rule overturns an interim policy that prohibited the dispensing of multiple prescriptions at a single office visit and clarifies the DEA's expectations, said Dr. Sitzman.

Under the new policy, physicians may write prescriptions labeled "do not fill until," with a preset date. This means patients can get a new prescription every 30 days, for 3 months, without having to return to the physician's office.

The prescriptions do not qualify as refills. They still must be taken to a pharmacy to be filled. DEA also said that the 90-day limit is the maximum according to its interpretation of congressional intent and the statute covering schedule II controlled substances.

In the rule, the DEA addressed several areas of concern to prescribing physicians.

The agency said it "wishes to dispel the mistaken notion among a small number of medical professionals that the agency has embarked on a campaign to 'target' physicians who prescribe controlled substances for the treatment of pain (or that physicians must curb their legitimate prescribing of pain medications to avoid legal liability)."

The agency noted that in any given year, fewer than 1 in 10,000 physicians lose their controlled substance registration because of a DEA investigation.

But, added the agency, the rule does not alter longstanding state and federal requirements that controlled substances can only be prescribed, administered or dispensed for a legitimate medical purpose by a physician acting in the usual course of professional practice.

The changes were first proposed in 2006, when the DEA was asked by commenters to issue specific guidance on how a clinician could assess pain, when a physician should prescribe an opioid, or how to use opioids.

But the agency said it would not do so, noting it does not regulate the practice of medicine and these topics are better addressed by professional organizations, medical schools, and postgraduate medical training.

Dr. Sitzman said the lack of strict guidelines is a positive thing.

Other organizations were also heartened by the rule change. In a statement, Dr. Rebecca Patchin, an American Medical Association board member, said the change "will give patients better access to the prescription drugs they need and continue to minimize the risks controlled substances pose to public health and safety." ■

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 tibiofemoral 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.

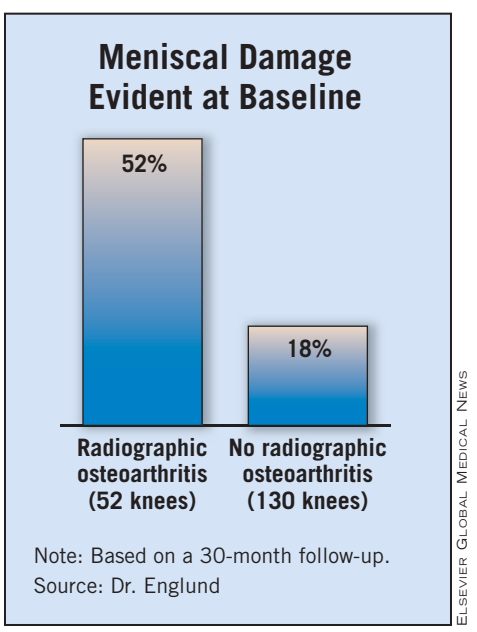
To assess the baseline meniscal status of the knees, two blinded musculoskeletal radiologists reviewed coronal and sagittal fast spin echo MRI images and evaluated each on a collapsed scale. Knees with no damage were grade 0, those with a minor tear were grade 1, and those with a nondisplaced tear, displaced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



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