## Repeated B-Cell Depletion Effective for Refractory SLE

BY ROBERT FINN
San Francisco Bureau

Repeated cycles of a combination of cyclophosphamide and rituximab proved effective in treating severe, recalcitrant systemic lupus erythematosus, according to a study by Kristine P. Ng, M.D., and colleagues at University College London (England).

The study involved seven refractory patients with SLE who underwent a total of 18 cycles of B-cell depletion, with 2 or 3 cycles per patient (Ann. Rheum. Dis. 2005 Nov. 3 [Epub doi.10.1136/ard.2005.044487]).

The regimen for each cycle involved two infusions of rituximab and intravenous cyclophosphamide given 2 weeks apart. One patient did not receive cyclophosphamide because of a previous allergy.

Routine immunosuppressives were stopped prior to the first cycle, but each cycle was accompanied by steroid cover. Mycophenolate was added in three patients after the third cycle, and in a fourth patient after the second cycle. One patient received methotrexate after the first cycle.

Four of seven patients improved clinically 4-6 months following the second cycle. Mean British Isles Lupus Assessment Group (BILAG) global scores dropped from 15 to 6 for all patients. The mean duration of response after the second cycle was 13 months, whereas the mean duration of B-cell depletion was 6 months.

Two of the four responsive patients improved clinically after the third cycle, with global BILAG scores dropping from 10 to 2 in one patient and from 27 to 6 in the other at 7 months. One of the patients relapsed 1 year later, and the other remained healthy without any immunosuppressives 13 months following the third cycle.

The study "gives us an extra leg up on the therapy of recalcitrant lupus, not only lupus nephritis but lupus everything," Robert Lahita, M.D., noted in an interview.

Dr. Lahita, a rheumatologist and vice president and chairman of medicine at Jersey City (N.J.) Medical Center, was not involved with the study. However, after hearing about the combination therapy at a recent meeting, he treated two recalcitrant SLE patients with rituximab and cyclophosphamide with good results.

"It has worked very nicely," he said. "The patients feel well, and the only drawback to the Rituxan [rituximab] therapy is maybe an allergic response on occasion. Cytoxan [cyclophosphamide] by itself is what we were using previously. We'd give Cytoxan every month for 6 months. And that gave you results, but it wasn't the same. [Rituxan] gives you a little bit of extra zip. It's like the perfect icing on the cake."

The downside is that some patients develop leukopenia, which necessitates discontinuing treatment until white cell counts rise back up to around 6,000-7,000 per mcL, he said.

"These are patients who don't respond to anything else and are near death as it is," Dr. Lahita said. "In most cases, these patients—the recalcitrant ones—would wind up getting bone marrow transplants. And that is really devastating because of the high mortality."

Dr. Lahita expects B-cell depletion to move beyond patients with highly recalcitrant SLE. "It's a safe treatment, and anything that's safe will be carried forward to other forms of the disease," he said.



