New guidance on how and when to stop immunosuppressants in lupus patients

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A new study presented today at the European League Against Rheumatism Annual Congress (EULAR 2014) showed that, for the majority of lupus patients who are in remission, it is possible to successfully stop immunosuppressant therapy without triggering a flare of their disease.1 Within two years, it was possible to stop the immunosuppressant in about 70% of clinically stable patients. Half were successful within three years, and this proportion remained stable for up to five years.1

Lupus is a chronic inflammatory disease that can affect any organ system, but mainly involves the joints, kidneys and skin.2 It typically follows a relapsing and remitting course; during a relapse, patients feel fatigue, and may develop rashes, arthritis (painful and swollen joints) and fever.2 Being able to stop long-term immunosuppressant therapy in a lupus patient without inducing a relapse is an important treatment goal because of the potential side effects of these drugs, including the increased risk of infection and cancer.

In the USA, the average incidence of SLE has been estimated to range between 1.8 and 7.6 cases per 100,000 person-years.3 Incidence rates in Europe are similar, ranging from 3.3 to 4.8 per 100,000 person-years. The incidence of SLE is greater in Afro-Americans compared with Caucasians.4 SLE affects 10 times as many women as men.2

Lupus patients who develop serious or life-threatening problems such as kidney inflammation, lung or heart involvement, and central nervous

system symptoms need more aggressive treatment, including high-dose corticosteroids such as prednisone, and immunosuppressants such as azathioprine (AZA), methotrexate (MTX) and mycophenolate mofetil (MMF).

"Until now, information on whether and how immunosuppressant therapy might be stopped in lupus patients after achieving low disease activity or remission has been limited," said lead author Dr Zahi Touma, Assistant Professor of Medicine, Clinician-Scientist, Division Of Rheumatology, University of Toronto, Canada.

"The results from our study provide useful guidance on how best to stop the immunosuppressant without triggering a flare. For example, patients who discontinued their immunosuppressant more slowly were less likely to flare within two years," Dr Touma explained. "Those lupus patients who were serologically active at the time the immunosuppressant was stopped were much more likely to flare on follow-up visits," he added.

Out of a total population of 1,678 patients registered at the Toronto Lupus Clinic, 973 had been prescribed an immunosuppressant; and 99 had stopped taking it, of which 56 had been on AZA, 25 on MTX, and 18 on MMF. Of the 99 patients who stopped their immunosuppressant, 25 flared within two years (16 on AZA; 7 on MTX and 2 on MMF; p=0.31); 17 patients experienced a flared after year two.

Comparing patients who flared within two years to those who did not, the percentage of patients with positive serology† at the time their immunosuppressant was stopped was greater in those who flared, 68% vs. 42% (p=0.04).

In the no flare group, the length of time from the start of tapering to stopping the immunosuppressant was 1.8±1.8 years, significantly slower than the 0.9±0.9 years in the group who did experience a flare

(p=0.002).

At the start of tapering, the mean age of the patients was 40.4±13.1 and mean disease duration was 11.4±9.4 years. 46 of the patients had follow-up available beyond two years; 32 were followed beyond three years, 26 beyond four years and 24 beyond five years. Using a Kaplan-Meier curve for the time to flare, at one, two, three, four and five years, the percentage of patients who flared was 17%, 30%, 46%, 49% and 51% respectively.

The analysis for this study was conducted on all patients seen in the Toronto Lupus Clinic in whom an immunosuppressant was tapered and then stopped. To be included, the lupus patient had to be in clinical remission: defined as no activity in the clinical SLE Disease Activity Index-2000 (SLEDAI-2K) descriptors‡ and an absence of proteinuria or lupus-related thrombocytopenia and leukopenia, and also to be taking ≤7.5mg of prednisone per day.

Three time points were identified for each patient:

- the start of tapering defined as the first visit with a decrease of at least 25% in the dose of immunosuppressant
- the day the immunosuppressant was completely stopped
- the end of the study - defined as the date of flare, or last clinic visit after the immunosuppressant was stopped.

Flare was defined as the introduction of a new immunosuppressant, or any increase of prednisone dosage in the context of clinically active lupus.

Flare was evaluated within the first two years from the immunosuppressant being stopped, and also at any time after the immunosuppressant was stopped.

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