# Biologic Therapy Complicates Vaccination for Travel

BY JOHN R. BELL
*Associate Editor*

Las Vegas — Solutions to several challenging treatment scenarios in patients undergoing biologic therapy for rheumatologic or dermatologic conditions were considered by a panel of experts at seminar sponsored by Skin Disease Education Foundation.

The head of the panel, Dr. Craig Leonardi, a dermatologist in private practice in St. Louis, presented one scenario in which a patient being treated with a biologic is about to travel abroad to a developing country for a brief visit and needs to get the recommended vaccinations. Among the questions he asked the panel: Should the patient get the vaccinations? If so, should he discontinue the biologic?

Discontinuing the biologic to get the vaccinations was deemed an option by the panel, but with caveats. "It depends on the agent," said Dr. Robert Kalb of the State University of New York at Buffalo. "If the person's on etanercept, and it's a short visit, [discontinuation is] certainly a very reasonable option. [If] the person's on efalizumab, I'd be a little bit more leery. The half-life of infliximab is such that, depending on the timing of the infusion, you might be able to get away with it." He noted that he advises continuing the biologic during vaccinations that use killed vaccine and thus there is no reason to stop therapy for influenza or pneumonia vaccinations.

Dr. Bruce Strober of New York University, New York, said that stopping the biologic makes it more likely the vaccine will be at its peak efficacy. "I think there are some tangential studies that show if you give some types of vaccines in the midst of biologic therapy, some immunologic readouts are reduced, but the clinical relevance of that hasn't been established." He noted that live vaccines are contraindicated with biologics. As to the length of time for biologic discontinuation in the setting of live vaccine use, "you would like the biologic to be more or less inactive in the patient, so four to five half-lives," he said.

**Should therapy be stopped prior to vaccinations? If it is a live vaccine, it depends on the biologic. For killed vaccines, there's no reason to stop biologic therapy.**

This estimate was shared by panelist Dr. Francisco Kerdel of Cedars Medical Center in Miami, who also raised the question of whether biologic treatment brings an increased risk of contracting disease, especially in regions with a greater number and variety of nefarious microbes. "When you talk about the granulomatous diseases being activated by the use of anti–[tumor necrosis factor], most of the time it applies to patients reactivating what they already have," he said.

Dr. Strober suggested that physicians ask patients taking biologics about their future travel plans and vaccinations.

Flare-up of the disease itself is one of the foremost risks of stopping a biologic, especially efalizumab, Dr. Leonardi noted. Disease rebound is less of a risk, however, with TNF-α antagonists.

Another challenging scenario that Dr. Leonardi presented involved an elderly patient with psoriatic arthritis and heart failure (HF) who is unwilling to accept conventional treatment and insists on biologic therapy.

"I think you need to define the severity of HF," Dr. Strober said, adding that studies of etanercept and infliximab showed that only patients with very severe heart failure experienced problems on infliximab, and only on the highest dose of 10 mg/kg. He advised consulting with a cardiologist to determine if tumor necrosis factor inhibitors are an option. Even so, he suggested trying efalizumab or alefacept first.

The panel also discussed the issue of weight and body mass index with biologic therapy. Morbidly obese patients don't respond as well to etanercept, Dr. Kalb noted, but the biologics with weight-based dosing, efalizumab and infliximab, have demonstrated similar responses in patients with and without high body mass index. Part of the difficulty in treating heavier patients may lie in weight-based dosing.

The final scenario presented involved a patient on a biologic who is about to undergo elective surgery for chronic cholecystitis refractory to antibiotics. Dr. Leonardi advised stopping the biologic and restarting it after surgery, except in the case of etanercept. Biologics might pose some effect on postsurgical wound healing and infection risk, but little is known about such interactions, Dr. Kerdel said.

It is important, however, to tell the surgeon what biologic the patient is taking, Dr. Leonardi said. "The surgeon may have no idea what these medicines are," he said.

Dr. Kalb noted that many patients with Crohn's disease need surgery and that many continue taking infliximab.

Dr. Kerdel noted that if the cholecystitis patient is taking efalizumab, "I would continue [treatment], because I think the risk of having a rebound phenomenon … would be greater than the risk of infections that we know of."

Dr. Leonardi is a consultant for Amgen, Abbott, Genentech, and Centocor. Dr. Kerdel is a consultant for Abbott, Amgen, and Centocor.

Dr. Kalb has been a consultant for the latter three firms, as well as for Genentech. Dr. Strober has received funding from, advised, or been a speaker for Genentech, Amgen/Wyeth, Centocor, Abbott, and Astellas.

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# Strong Link Between Gout, Metabolic Syndrome Found

BY LUANN DALLOJACONO
*Contributing Writer*

The prevalence of metabolic syndrome may be nearly three times higher among individuals with gout, compared with unaffected individuals, judging from results of a recent data analysis.

A link between gout and metabolic syndrome has been suggested by other investigators, but the degree of the overlap between the two conditions has remained unclear, according to study investigators Dr. Hyon K. Choi of the Arthritis Research Centre of Canada and his associates.

A total of 8,807 individuals aged 20 years or older participated in the third National Health and Nutrition Examination Survey (NHANES-III) from 1988 to 1994. A total of 233 had gout, according to self-report (mean age of 58 years). All individuals were assessed for metabolic syndrome; the condition was deemed to be present if an individual had at least three of the following five metabolic abnormalities: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, high blood pressure, and high fasting glucose.

Prevalence of metabolic syndrome was approximately 63% among the 233 individuals with gout and 25% among 8,574 individuals without gout. The prevalence rates of each of the five metabolic abnormalities associated with metabolic syndrome were higher among adults with gout. The prevalence of high blood pressure in individuals with gout (69%) was more than double the prevalence of those without. The link between metabolic abnormalities and gout was evident across subgroups of major associated gout risk factors including body mass index, hypertension, and diabetes, the investigators reported (Arthritis Rheum. 2007;57:109-15).

The interplay between hyperuricemia and high insulin levels caused by insulin resistance may explain the connection. Prevalence of hyperuricemia was 49% among individuals with gout and 18% among those without, according to the analysis by Dr. Choi and his associates.

Prevalence of metabolic syndrome increased from 27% among participants with gout aged 20-39 years to 72% among participants aged 40-59. Prevalence of metabolic syndrome among individuals without gout increased from only 12% in adults aged 20-39 years to 31% in those aged 40-59 years Prevalence for metabolic syndrome in adults over age 60 years with gout (71%) was more substantial than in those without gout (49%).

The study was funded by TAP Pharmaceutical Products Inc. and Savient Pharmaceuticals Inc. Dr. Choi reported receiving consulting fees from both companies. ■

# *DMARDs Ineffective for Recent-Onset RA After Initial Methotrexate Failure*

BY MELINDA TANZOLA
*Contributing Writer*

Individuals with recent-onset rheumatoid arthritis treated according to disease activity score for 2 years appear to gain little benefit from conventional disease-modifying antirheumatic drugs after initial methotrexate failure, according to the results of a post hoc analysis of the randomized, multicenter, controlled BeSt study.

Overall, 162 of the 244 study patients (66%) failed 2 years of initial methotrexate (MTX) therapy. A subsequent addition of, or switch to, sulfasalazine (SSA), failed in 108 of 138 patients (78%). Subsequent leflunomide monotherapy failed in 47 of 54 patients (87%), while MTX plus SSA and hydroxychloroquine failed in 28 of 44 patients (64%), reported Dr. Sjoerd M. van der Kooij of the Leiden (the Netherlands) University Medical Center and colleagues. However, 34 of 48 patients (71%) who switched to MTX plus infliximab did have treatment success.

Overall, the median total Sharp/van der Heijde score progression was significantly greater among "MTX failures" than "MTX successes" (3 units vs. 1 unit, respectively), regardless of response to subsequent disease-modifying antirheumatic drugs (DMARDs) (Ann. Rheum. Dis. 2007 Feb. 9 [Epub doi:10.1136/ard.2006.066662]).

"This observation confirms earlier studies suggesting that adequate, early suppression of disease activity is paramount for the suppression of joint damage progression," wrote Dr. van der Kooij and colleagues.

"MTX successes" included the 79 patients who achieved a disease activity score (DAS) of 2.4 after 2 years of methotrexate monotherapy. "MTX failures" included the 66% of patients in the study who initially received MTX 15-25 mg/wk but who discontinued the drug because of toxicity or failure to achieve a DAS of 2.4 or less after 2 years, according to the investigators. These patients were then randomized to receive either sequential monotherapy or a step-up combination therapy. A higher DAS at baseline and female sex were significantly and independently predictive of MTX failure.

Dr. van der Kooij and colleagues suggested that, following the failure of initial MTX therapy, treatment with an anti–tumor necrosis factor agent should not be delayed, given that "switching to or adding other conventional DMARDs offers little chance of clinical efficacy and allows progression of joint damage."

BeST is supported by the Dutch government and the Dutch College of Health Insurance Companies. ■