were used in the model: discontinuation rate for triple therapy [0.22, (range, 0.11 to 0.46)] and etanercept [0.10 (range, 0.07 to 0.15)], annual cost of triple therapy [$791 (range, $500 to $1200)] and etanercept [$24,446 (range, $12,000 to $26,000)], mean income [$45,552 (range, $30,000 to $60,000)], discounting of 3% (0% to 5%), and quality-of-life mapping using the EQ-5D. At both 1 and 2 years the IT group had the lowest cost and greatest effectiveness. When the model was extended to lifetime, both the IT and IE treatment groups were cost effective, with an incremental cost effectiveness ratio (ICER) of ~$840,000/QALY.

A sensitivity analysis indicated that the results were the most sensitive to etanercept cost and decreases in the discontinuation rates of triple therapy, but these findings did not change the overall conclusions. "The benefits from all strategies were comparable, but biologics strategies were almost twice as expensive as triple strategies, producing ICERs greater than what most healthcare settings find acceptable," concluded Dr. Michaud.

Early Results Indicate Rituximab Effective in the Treatment of IgG4-Related Disease

Written by **Muriel Cunningham**

Immunoglobulin G4-related disease (IgG4-RD) is a fibro-inflammatory disorder that was first described 10 years ago. IgG4-RD may affect multiple organs and resembles other diseases such as Sjögren's syndrome, lupus, sarcoidosis, lymphoma, and idiopathic membranous glomerulonephropathy. This disorder is typically treated with steroids but the response is mixed: some patients experience a complete response but others cannot completely discontinue steroid therapy. John H. Stone, MD, MPH, Massachusetts General Hospital, Boston, Massachusetts, USA, gave an overview of the results of a prospective open-label investigator-initiated trial of rituximab in the treatment of IgG4-related disease [NCT1584388].

Thirty patients were enrolled at two centers and received rituximab 1000 mg intravenously in two doses. The use of steroids was minimized by having patients taking steroids at baseline and taper off within the first 2 months. The primary outcome measure was the disease response at 6 months, defined as a decline in the IgG4-RD Responder Index (IgG4-RD RI) of at least 2 points without concomitant prednisone use. Flow cytometry analyses were also conducted at one of the sites.

The mean age of the patients was 63 years (range, 42 to 82 years) and 26 (87%) were male. Ten of 30 (33%) had normal serum IgG4 concentrations at baseline with a wide range in obtained values (26 to 4780 mg/dL). The most common organs involved (≥50%) were the pancreas, salivary glands, and lymph nodes. Twenty-six patients were followed for 6 months and were included in the primary analysis. Of these 26 patients, 24 (92%) met the primary outcome. The mean IgG4-RD RI score at baseline fell from 12 to 2.1 at 6 months ($p<0.01$). The mean Physician's Global Assessment (PGA) at baseline was 63 mm and, by the 6-month time point, 73% of completed patients had improved to a PGA of 0 mm. In addition, a significant decrease of serum IgG4 concentration was observed, from a baseline mean of 609 to 293 mg/dL ($p<0.001$).

Overall, 90% of patients had controlled disease without prednisone and three patients achieved disease control by adding prednisone. Of the three that added prednisone, two achieved complete remission and the remaining patient was unable to completely discontinue prednisone. Five patients relapsed, one occurring before the 6-month time point. Seven serious adverse events were reported but none were considered related to rituximab.

The flow cytometry results were striking, showing a large peripheral plasmablast expansion at baseline in all IgG4-RD patients that were tested. These increases occurred even when serum IgG4 concentrations were within the normal range. The number of plasmablasts decreased dramatically within 4 weeks of rituximab treatment.

The results from this mechanistic study suggest that plasmablast elevations may be a useful biomarker in monitoring patients with IgG4-RD. "Rituximab appears to be a highly effective therapy for IgG4-RD. This medication has an important role in IgG4-RD that is refractory to steroids and for patients in whom steroids are contraindicated," concluded Dr. Stone.