AMBITION was a randomized, double-blind, placebo-controlled, phase 3 study in patients with active moderate to severe RA of at least 3 months duration who were MTX-naïve or had not received MTX for at least 6 months before randomization and had not previously failed MTX or biologic treatment. Additional inclusion criteria included: swollen joint count ≥6 (of 66) and tender joint count ≥8 (of 68) at screening/baseline and CRP ≥1.0 mg/dL or ESR ≥28 mm/hr. Patients were randomly assigned to receive either tocilizumab 8 mg/kg every 4 weeks plus placebo capsules weekly or placebo infusions every 4 weeks plus methotrexate (7.5 mg/week titrated to 20 mg/week within 8 weeks).

After 24 weeks of treatment, 70% of tocilizumab patients achieved a 20% improvement in their symptoms versus 53% of MTX patients (p<0.0001; Figure 1). Significant differences in favor of tocilizumab also were seen on ACR50 and ACR70 responses (Table 1). A higher proportion of patients who received tocilizumab achieved a good/moderate EULAR response as early as Week 2 (64% vs 19% MTX).

Mean change in CRP levels from baseline to Week 24 was -2.6 mg/dL for tocilizumab versus -1.9 mg/dL for MTX. The incidence of adverse events (AEs) was similar (80% tocilizumab; 78% MTX). AEs that led to withdrawal were more common in the MTX arm (5.3% vs 3.8% for tocilizumab). Serious AEs were higher with tocilizumab (4% vs 3% for MTX), as were serious infections (1.4% vs 0.7% for MTX), but these differences were not statistically significant. Shifts in ALT from normal at baseline to >3x ULN occurred more frequently in the MTX arm (4%) compared with tocilizumab (2%). Shifts in total cholesterol from <200 to >240 mg/dL occurred more frequently with tocilizumab (13% vs <1% for MTX).

Figure 1 ACR 20, 50, and 70 Response Rates at Week 24.

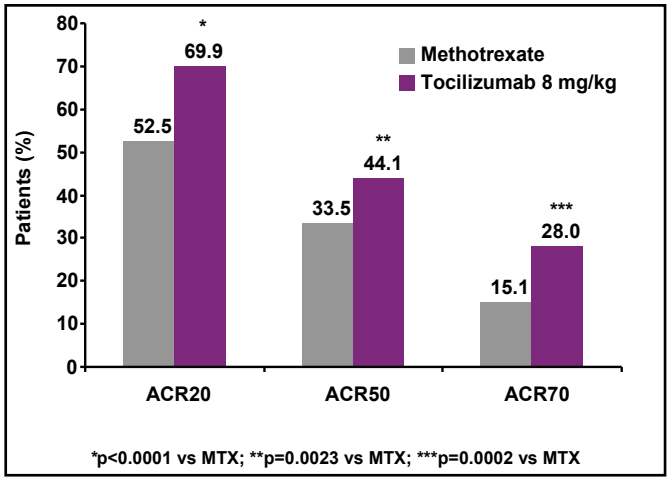

Table 1: Results at Week 24 (ITT population).

	Tocilizumab n=286	Methotrexate n=284	p value
ACR20 response	70%	53%	p<0.0001
ACR50 response	44%	34%	p=0.0023
ACR70 response	28%	15%	p=0.0002
Patients with DAS28<2.6	34%	12%	-
Mean change in DAS28	-3.3	-2.2	-
Mean change in HAQ-DI	-0.7	-0.6	-

"We are very encouraged by the results of the AMBITION study, which shows for the first time that treatment with a single biologic agent is superior to methotrexate at 6 months of therapy," said Prof. Jones. "Overall, these compelling results further establish the efficacy and safety of tocilizumab in treating the chronic signs and symptoms of rheumatoid arthritis that dramatically affect the lives of patients."

Results of the GO-AFTER Study

Josef S. Smolen, MD, PhD, Medical University of Vienna, Vienna, Austria, presented data from the GO-AFTER Study (NCT00264550), the first prospective, randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of a TNF inhibitor (golimumab) in patients with active rheumatoid arthritis (RA) who were previously exposed to another TNF inhibitor.

In this study, patients with a diagnosis of active RA (ACR criteria, duration ≥3 months; ≥4 tender joints and 4 swollen joints) who had received at least one dose of a biologic TNF-blocker but discontinued treatment for any reason were randomly assigned to receive placebo (n=155) or golimumab 50 mg (n=153) or 100 mg (n=153) subcutaneously every 4 weeks. Patients could continue to receive stable doses of methotrexate, sulfasalazine, and/or hydroxychloroquine if they were receiving them at baseline. The primary study endpoint was the proportion of patients who achieved ACR20 at Week 14.

Patients were predominately women who had a median age of 55 years and median disease duration of 8.65 to

9.80 years. Two-thirds (66%) of patients had received one anti-TNF agent, 25% had received 2, and 9% had received 3. Prior anti-TNF therapy had been discontinued due to lack of efficacy in 58% of patients.

At Week 14, significantly ($p<0.001$) more patients who were treated with golimumab achieved ACR20 versus placebo-treated patients. These results essentially were maintained at Week 24. Golimumab also was significantly more effective than placebo in the subgroup of patients whose prior anti-TNF-alpha therapy had been discontinued due to lack of efficacy (36% golimumab 50 mg and 43% golimumab 100 mg vs 18% placebo; $p=0.006$ and $p<0.001$, respectively).

The percentage of patients who achieved ACR50 and ACR70 at Week 24 was significantly higher ($p\leq0.01$) with golimumab versus placebo (18.3% and 20.3% vs 5.2% and 11.8% and 10.5% vs 3.2%; ACR50 and ACR70, golimumab 50 mg and 100 mg vs placebo, respectively). These results are similar to those that were seen in trials that included other biologics and methotrexate [Genovese MC et al. *New Engl J Med* 2005; Cohen SB et al. *Arthritis Rheum* 2006].

Golimumab was generally well tolerated (Table 1) and demonstrated a safety profile that was similar to other anti-TNF agents. Antibodies to golimumab were detected in 3.0% of golimumab-treated patients.

"Our findings show that golimumab holds great promise in various RA patient populations, including those patients who have previously discontinued other TNF inhibitors," said Prof. Smolen.

Table 1. Summary of Safety Events Through Week 24 (% of Patients).

	Placebo	Golimumab 50mg	Golimumab 100mg	Golimumab All
Adverse events	72.3	66.4	78.3	68.1
Serious adverse events	9.7	7.2	4.6	5.9
Infections	32.9	34.9	36.2	32.4
Serious infections	3.2	3.3	0.7	1.9
Injection site reactions	3.9	5.9	10.5	8.0

Randomized Controlled Trials of Epratuzumab Reveal Clinically Meaningful Improvements in Patients with Moderate/Severe SLE Flares

Michelle Petri, MD, MPH, Johns Hopkins University, Baltimore, MD, reported the results of 2 48-week, randomized, double-blind, placebo-controlled clinical trials that evaluated the humanized anti-CD22 monoclonal antibody epratuzumab for the treatment of patients with severe BILAG A or moderate BILAG B (in ≥2 organ systems) SLE flares.

Patients were randomly assigned to receive placebo (n=37), epratuzumab 360 mg/m^2 (n=42), or epratuzumab 720 mg/m^2 (n=11) infusions for up to 4 treatment cycles. Corticosteroids were increased by ≥10 mg daily at baseline. Other SLE-specific therapies remained unchanged. Systematic tapering of corticosteroids was started at Week 4 with the aim of achieving a reduction in daily corticosteroid doses to ≤10 mg daily (Study 1) or ≤7.5 mg daily prednisone equivalents (Study 2) by Weeks 20-24. The primary study endpoint was reduction at Week 12 of all BILAG A to B and BILAG B to C, no worsening in other systems, and no addition or increase in immunosuppressives and/or anti-malarials or corticosteroids above baseline or specified taper levels. These studies were prematurely discontinued due to study drug supply interruption, and the data from the 2 trials were combined for analysis. Patients were followed for 6 months after enrollment or cessation of dosing. Patients had varying lengths of study participation and numbers of doses.

Patients were predominately women (94%), who had a mean age of 36.8 years. At baseline, >40% of patients had BILAG A, and 91% had >2 BILAG As or Bs with a mean total BILAG score of 13.2. Over 60% were receiving immunosuppressives; 43% of patients were receiving >25 mg/day corticosteroids.

Epratuzumab at both doses resulted in greater reductions in total BILAG scores versus placebo, and the probability of achieving a sustained response prior to Week 12, 24, and 48 was greater with epratuzumab treatment (Figure 1A and B). Patients who received epratuzumab were twice as likely as placebo-treated patients to achieve sustained improvement in BILAG scores (HR 2.18; $p=0.021$; Table 1). BILAG scores and global disease assessments of disease activity at Week 12 are summarized in Table 1. Cumulative corticosteroid use over 24 weeks was lower in epratuzumab-treated patients versus placebo-treated patients.