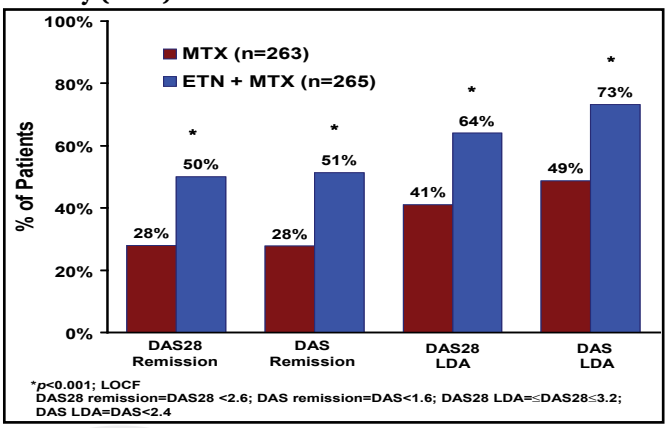
achieving HAQ ≤0.5 was significantly (p<0.001) greater in the combination group (55%, 140/256) versus the MTX group (39%, 93/241).

Figure 1. DAS28 and DAS Remission and Low Disease Activity (LDA).



Serious adverse events were reported by 33 patients (12%) in the combination group and 34 (13%) in the MTX group. There were no differences in the rates of serious infections or malignancies and no cases of tuberculosis or demyelinating disease.

"Until recently, we did not know whether remission was a realistic", said Prof. Emery. "We now have results which show that not only is clinical remission achievable in a significant number of patients, but radiographic and functional remission are also achievable. These exciting results lead to the next therapeutic step in aiming for multiple measures of remission as our treatment goal, no longer just one".

Effect of Previous Bisphosphonate Use on Response to Zoledronic Acid

The HORIZON Pivotal Fracture Trial (NCT00049829) was a 3-year, double-blind, randomized, placebo-controlled trial in which patients received a 15-minute infusion of zoledronic acid 5 mg (n=3889) or placebo (n=3876) at baseline and at 12 and 24 months. Results, previously reported by Black and colleagues, showed that once-yearly zoledronic acid significantly reduces the risk of vertebral, hip, and other fractures [Black D et al. *N Engl J Med* 2007].

Richard Eastell, MD, PhD, University of Sheffield, Sheffield, UK, presented the results of a planned subanalysis from HORIZON that evaluated the effect of prior bisphosphonate use on the primary endpoints of new vertebral fracture (in patients who were not taking concomitant osteoporosis medications) and non-vertebral fractures (in all patients). Markers of bone turnover were also evaluated.

Bisphosphonates had been used by 565 patients (14.5%) in the zoledronic acid group and 557 patients (14.4%) in the placebo group. The duration of the washout period was dependent on previous use (eg, 2 years if previous use was ≥48 weeks).

Over 3 years, the incidence of vertebral fracture was significantly (p<0.0001) lower in the zoledronic acid group versus the placebo group regardless of prior bisphosphonate.

Significant (p<0.001) reductions in the incidence of non-vertebral fractures also were seen in bisphosphonate-naïve patients who were treated with zoledronic acid (n=237, 7.60%) versus placebo (n=337, 10.88%), but not in patients who previously had used bisphosphonates (n=54, 10.11% vs n=50, 9.80%).

Over 3 years, changes in markers of bone turnover were similar between the bisphosphonate use groups. Reductions from baseline at Month 36 in serum levels of c-telopeptides, bone alkaline phosphatase, and N-terminal propeptide of type I collagen with zoledronic acid relative to placebo were 53.8%, 30.0%, and 48.4%, respectively, in the bisphosphonate-naive group, and 49.3%, 16.1%, and 50.1%, respectively, in the previous bisphosphonate use group.

The benefits of once-yearly zoledronic acid that were observed during a 3-year period were robust on vertebral fractures, bone turnover markers, and bone mineral density, regardless of whether patients had previously received bisphosphonate treatment. Zoledronic acid had a favorable safety profile and generally was well tolerated.

The AMBITION Study

Although studies have shown current anti-TNF treatments to be superior to short-term methotrexate (ie, before 24 weeks), none has shown superiority at Week 24. Graeme Jones, MD, PhD, University of Tasmania, Hobart, Australia, lead investigator of the AMBITION study (NCT00109408), presented data that showed that after 24 weeks, tocilizumab (an anti-IL-6 receptor antibody that inhibits IL-6 signaling) monotherapy was clinically superior to methotrexate (MTX) monotherapy in patients with rheumatoid arthritis (RA) who have not failed previous MTX or biologic treatment.

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.

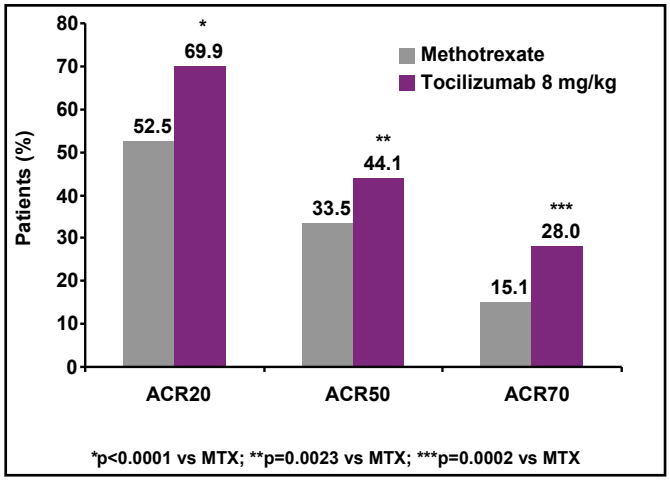


Table 1: Results at Week 24 (ITT population).

	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