randomized to 1 of the CZP arms, following a loading dose. The primary efficacy endpoints were ACR20 response at Week 12 and change from baseline in the modified Total Sharp Score (mTSS) at Week 24 (mTSS results were not reported at the meeting). Key secondary endpoints included: ACR20 response and change from baseline in Health Assessment Questionnaire-Disease Index (HAQ-DI) at Week 24, the Psoriasis Area and Severity Index (PASI) 75 response at Week 24 in the subgroup of subjects with psoriasis involving ≥ 3% body surface affected (BSA) at baseline, and change from baseline in mTSS at Week 48.

Subjects were aged 47 to 48 years, evenly divided between men and women, and overweight (body mass index 29.2 to 30.5 kg/m^2). Approximately 20% of patients had prior anti-TNF exposure. Subjects had significant disease, as evidenced by the SJC (mean 10.4 to 11.0/66), TJC (mean 19.6 to 21.5/68) the presence of enthesitis in >60% of subjects and dactylitis in approximately one-third of subjects. The median baseline PASI score for subjects was 7.0 to 8.1.

At Week 12, 58% of patients who received CZP 200 mg every 2 weeks and 51.9% of those who received CZP 400 mg every 4 weeks achieved an ACR20 response compared with 24.3% of patients who were receiving placebo (p<0.001). More CZP-treated patients in both groups also achieved ACR50 and ACR70 response compared with placebo (Figure 1). Results were observed as early as Week 1. Functional improvement was significant (p<0.001) for subjects who received CZP, with both groups reporting changes in HAQ-DI scores at Week 24 that exceeded the minimally important difference of 0.35 [Mease P et al. *J Rheumatol* 2011]. Although the response was slightly slower, treatment with CZP was associated with a robust skin response (Table 1).

Figure 1. ACR Response at Week 12.
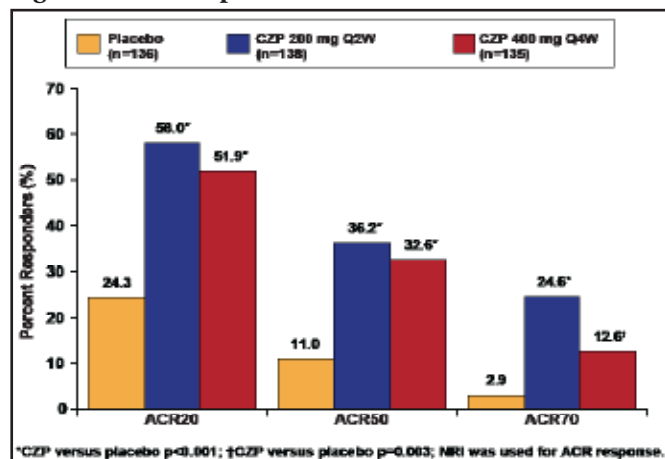
combined CZP group, and serious adverse events occurred at 4% for the placebo group versus 7% for the combined CZP group. Two deaths occurred during this phase of the study, but neither was considered to be related to the study drug.

Table 1. PASI 75 and 90 Response.

	CZP 200 mg Q2W (n=90)		CZP 400 mg Q4W (n=76)		Placebo (n=86)	
	Week 12	Week 24	Week 12	Week 24	Week 12	Week 24
PASI75	46.7*	62.2*	47.4*	60.5*	14.0	15.1
PASI90	22.2*	46.7	19.7**	35.5*	4.7	5.8

*p<0.001 vs placebo; **p=0.004 vs placebo; PASI=Psoriasis Area and Severity Index; CZP=certolizumab pegol; Q2W=every 2 weeks; Q4W=every 4 weeks.

Efficacy and Safety of NNC0109-0012 (anti-IL-20 mAb) in Patients with RA: Results from a Phase 2a Trial

Written by Maria Vinall

Elevated expression of interleukin-20 (IL-20) and its receptors has been demonstrated in synovium from patients with rheumatoid arthritis (RA) and is thought to be implicated in the pathogenesis of RA. NNC0109-0012 is a novel human monoclonal IgG4 antibody that binds to and neutralizes the activity of IL-20. Results of a Phase 2 study, presented by Ladislav Šenolt, MD, PhD, Institute of Rheumatology, Prague, Czech Republic, suggest that IL-20 is a potential target for RA therapy.

The primary objective of this randomized multicenter, double-blind, multiple-dose, placebo-controlled Phase 2a trial was to evaluate the change in disease activity (DAS28-CRP) following 12 weeks of treatment with NNC0109-0012 in patients with active RA. Secondary objectives included EULAR and ACR20/50/70 responses and safety, pharmacokinetics (PK), pharmacodynamics (PD), safety, tolerability, and immunogenicity. Subjects were required to be aged 18 to 75 years with active RA (DAS28-CRP ≥4.5; ≥5 swollen and ≥5 tender joints of the 28-joint count), have a disease duration ≥3 months, and have been on stable methotrexate therapy (≥7.5 to ≤25 mg/week) for at least 4 weeks prior to randomization.

The safety profile of CZP was similar to that observed in patients with rheumatoid arthritis. Adverse events occurred at rates of 68% for the placebo group versus 69% for the

A total of 67 patients (mostly women, two-thirds rheumatoid factor [RF]- and anticitrullinated protein antibody [ACPA]-positive, mean DAS28-CRP score of 6.0; Table 1) with active RA were randomized to subcutaneous NNC0109-0012 3 mg/kg once weekly for 12 weeks (n=45) or placebo (n=22) along with standard methotrexate treatment and followed for an additional 13 weeks.

Table 1. Demographics.

	Placebo n=22	NNC0109-00121 n=45
Age, years*	51.1 (28; 65)	50.9 (26; 75)
Women/Men, %	72.7/27.3	77.8/22.2
Duration of RA years*	6.1 (0.4; 16.2)	6.8 (0.5; 17.3)
Duration of MTX therapy, years*	1.9 (0.1; 7.0)	1.9 (2.0; 14.3)
RF-positive, %	63.6	71.1
ACPA-positive, %	68.2	68.9
RF- and ACPA-positive, %	63.6	64.4
DAS28-CRP*	6.0 (3.8; 7.3)	6.0 (3.9; 7.8)
DAS28 Components*		
Tender joints (28)	16.0 (5.0; 28)	17.5 (5.0; 28)
Swollen joints (28)	11.5 (5.0; 24)	13.0 (5.0; 24)
Subject's VAS (cm)	7.1 (2.6; 8.7)	6.9 (0.4; 9.7)
CRP (mg/L)	9.4 (0.6; 77.8)	7.2 (0.8; 69.5)

*Mean (min; max); ACPA=anticitrullinated protein antibody; CRP=C-reactive protein; DAS=disease activity score; MTX=methotrexate; RA=rheumatoid arthritis; RF=rheumatoid factor; VAS=visual analog scale.

At 12 weeks, mean changes in DAS28-CRP were significantly greater for NNC0109-0012 compared with placebo (difference, -0.88; 95% CI for difference, -1.61 to -0.14; p=0.020). Significant reduction of disease activity (-0.5; p=0.011) was observed after 1 week and was maintained for 5 weeks after the end of treatment. The reduction in disease activity was observed primarily in RF- and ACPA-positive patients. Estimated mean difference at 12 weeks was -1.66 [-2.53; -0.79; p=0.0004] and was driven mainly by a reduction in tender and swollen joints. There were no differences for DAS28-CRP changes between anti-IL-20- and placebo-treated patients with seronegative disease.

On the secondary endpoints, treatment with NNC0109-0012 resulted in a significant percentage of subjects who achieved moderate or good EULAR response (75.5%) compared with placebo (54.5%) after 12 weeks of treatment (p=0.02). DAS28-CRP remission (≤2.6) was achieved by approximately 18% of NNC0109-0012 patients. ACR 20/50/70 responses were also significantly higher in NNC0109-0012-treated RF- and ACPA-positive patients, compared with placebo-treated patients (p=0.028, p=0.045 and p=0.018, respectively), although the trial was not powered to detect differences in ACR20/50/70 responses.

The occurrence of adverse events (AEs) was similar in both groups. There was 1 withdrawal because of AEs in the placebo group. Severe AEs were reported by 1 subject in each group. There were more infections in the active treatment group (10 events in 10 patients) compared with placebo (2 events in 1 patient), but only 3 were considered to be related to the study drug. The infections were mild and consisted of upper respiratory and urinary tract infections, bronchitis, herpes simplex, and herpes zoster (placebo). Four patients in the active treatment group experienced mild, reversible injection-site reactions. No deaths, serious AEs, or dose-limiting toxicities were reported.

24-Week Data from the Phase 4 ADACTA Trial

Written by Maria Vinall

Data from several registries and a United States health insurance claims database have shown that approximately one-third of rheumatoid arthritis (RA) patients are being treated with biologics as monotherapy [Yazici Y et al. *Bull NYU Hosp Jt Dis* 2008; Lee SJ et al. *J Rheumatol* 2009], but there have been no head-to-head studies to assist in the choice of monotherapy for these patients. Results from the Multi-center, Randomized, Blinded, Parallel-group Study of the Reduction of Signs and Symptoms During Monotherapy Treatment With Tocilizumab 8 mg/kg Intravenously Versus Adalimumab 40 mg Subcutaneously in Patients With Rheumatoid Arthritis trial [ADACTA; NCT01119859], presented by Cem Gabay, MD, University Hospitals, Geneva, Switzerland, suggest that tocilizumab monotherapy may be more effective than adalimumab monotherapy reducing the signs and symptoms of RA.

The ADACTA trial was an international, multicenter, randomized, double-blind, 24-week superiority trial that compared tocilizumab with adalimumab monotherapy in patients with RA. Patients were required to have an RA diagnosis of ≥6 months and a Disease Activity Score (DAS) score >5.1 and to be methotrexate-intolerant or judged inappropriate for continued treatment with methotrexate. Patients with prior treatment with a biologic agent were excluded. The primary study endpoint was mean change from baseline in the DAS28 at Week 24. Key secondary endpoints included efficacy at Week 24, based on the proportions of patients who achieved DAS28 remission (<2.6) and low disease activity (≤3.2), ACR 20/50/70 responses, and ACR/EULAR remission. Safety was assessed using adverse events (AEs) and laboratory parameters. Clinical Disease Activity Index (CDAI) responses were assessed as a *post hoc* analysis.

Study participants, aged 53 to 54 years and mainly women (82% in the adalimumab arm; 79% in the tocilizumab arm), had active disease (DAS 6.7 to 6.8; Health Assessment Questionnaire score 1.6 to 1.7) and a disease duration of 6.3 to 7.3 years. Subjects were randomized to intravenous