MAGNETIC RESONANCE IMAGING MAY BE HELPFUL IN PREDICTING LONG TERM EFFICACY OF CERTOLIZUMAB PEGOL IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background

Certolizumab pegol (CZP) has previously been shown to improve signs and symptoms of rheumatoid arthritis (RA) in a diverse group of patients, including 37.6% who previously used a TNF inhibitor[1]. CZP has also been shown to inhibit radiographic progression[2].

Objectives

The study, THE EFFECT OF CERTOLIZUMAB PEGOL IN COMBINATION WITH METHOTREXATE ON MRI SYNOVITIS AND BONE EDEMA AND PATIENT REPORTED OUTCOMES AS MEASURED USING AN AUTOMATED VISIT MANAGER SYSTEM IN MODERATE TO SEVERE RA PATIENTS (**PICS**), evaluated the efficacy of CZP in combination with methotrexate (MTX) in reducing synovitis and osteitis assessed by non-contrast MRI in patients with moderate to severe RA, who failed at least one non-biologic or biologic DMARD. Value of short-term MRI findings for predicting long-term efficacy of CZP was also assessed.

Methods

In this 2-center open-label study, 20 adult RA pts with DAS > 4.4, on stable dose of MTX, received CZP 400 mg at wk 0, 2 and 4, followed by 200 mg every two wks for 52 wks.
All patients had unilateral hand and wrist non-contrast MRI using 0.2 T extremity scanner at baseline, 6 wks, 16 wks and 52 wks. Images were scored according to the RAMRIS system[3] and 9-point cartilage loss (CL) scale[4] by a radiologist blinded to visit order.
Bilateral hand and foot radiographs were taken at baseline, 16 wks and 52 wks and scored according to the van der Heijde-Sharp system.

Results

16/20 pts completed 52 wks. No serious adverse events were reported. DAS28 and RAPID scores were significantly reduced at all time points compared with baseline (Wilcoxon; $p<0.001$) (Figure 1).
ACR20/50/70 response rates at 16 & 52 wks (with non-completers considered non-responders) were 60/30/15 & 45/30/20%, respectively. 80% at wk 12 and 69% at wk 52 achieved moderate or good EULAR response. Only one pt achieved low disease activity at wk 52. 80% of patients had a DAS28 improvement of ≥ 1.2 by wk 12. Of these, 25% did not achieve EULAR response at wk 52. None of the remaining 20% of patients with DAS28 improvement < 1.2 by wk 12, had EULAR response at wk 52.

Mean (SD) age (years)	52.2 (16.9)
Number (%) of females	14 (70)
Mean (SD) disease duration (years)	7.3 (5.6)
Number (%) RF+	10 (50)
Number (%) anti-CCP+	12 (60)
Mean (SD) MTX dose (mg/wk)	17.25 (3.0)
Mean (SD) Prednisone dose (mg/day)	2.5 (5.0)
Number (%) previously on a biologic	17 (85)
Mean TJC (out of 68)	34
Mean SJC (out of 66)	16
Mean (SD) ESR	40.0 (34.8)
Mean (SD) CRP (mg/L)	3.6 (2.7)
Mean (SD) HAQ	4.38 (1.68)
Mean (SD) DAS28	6.60 (1.06)
Mean (SD) DAS28 CRP	5.74 (0.66)

Table 1: Baseline Characteristics

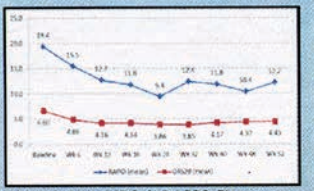

Figure 1: RAPID3 & DAS28 Changes from Baseline

Whereas trends towards worsening erosion (ERO) and cartilage loss (CL and JSN) on MRI (Fig 2) and radiography (Fig 3) despite improvement in MRI synovitis (SYN) and osteitis (OST) were evident, statistically significant changes from baseline in mean scores were not observed, most likely due to the small number of patients.

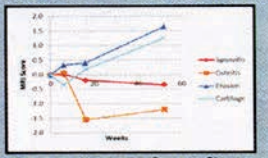

Figure 2: Mean MRI Scores Changes

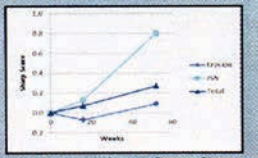

Figure 3: Mean Sharp Score Changes

52-wk EULAR responders had significantly greater improvement in the OST scores at 16 wks than non-responders did ($p=0.043$). Changes in SYN, ERO or CL scores did not differ significantly between the two groups (Figure 4). All pts who had improved OST scores by wk 16, were clinical responders at wks 12 and 52. Clinical responders at wk 12 had 73% probability of EULAR response at wk 52, but if they also had OST improvement at wk 16, the probability was 100% (PPV=1.0). Conversely, if OST worsened, the probability EULAR response at 52 wks was only 33% (NPV = 0.66).

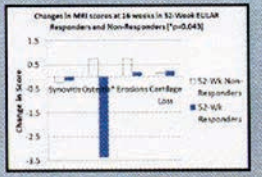

Figure 4: 16-wk MRI Score Changes between 52-wk Clinical Responders and Non-responders

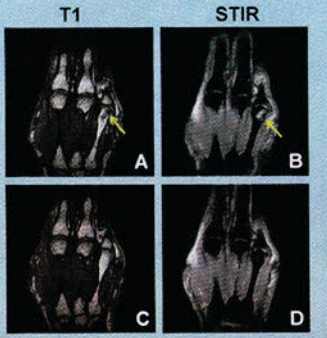

Figure 5: MRI of the right hand at baseline (A, B) and wk 16 (C, D) shows improvement of osteitis (arrows) in the fourth metacarpal head. The patient was a clinical responder at wks 12 and 52.

Conclusion

In this open-label study of active RA patients who failed at least one DMARD, usually a biologic, improvement of osteitis on MRI predicted long-term clinical response to CZP.
This finding may be useful for guiding therapeutic choices in patients with RA who have previously used a biologic.
Larger studies should be done to confirm these findings.

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References

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4. Peterfy C, et al. *Arthritis Res Ther.* 2012