



A Pilot Study of 10 Patients Measuring High and Low Field MRI on Patients With Rheumatoid Arthritis

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ABSTRACT

Background: Abatacept has been shown to reduce osteitis and erosions in patients with RA¹. Low and high field MRI systems have independently been shown to be sensitive to the measurement of osteitis and erosions in RA patients (pts)².

Objectives: To explore the comparative capabilities of low (0.28T) vs. high (1.5T) field MRI in the detection of changes in wrist and hand findings following treatment with abatacept with MTX in RA.

Methods: Ten RA pts who had been unresponsive to either MTX alone or in conjunction with an anti-TNF agent with either osteitis or erosions on baseline MRI were treated for 26 weeks with abatacept infusions on days 1, 15, 28, and every 28 days thereafter. 0.28T and 1.5T MRI scans of the wrist and hand were obtained at weeks 0, 4 and 26 and scored by 2 blinded radiologists using OMERACT/RAMRIS system. Imaging results were compared with clinical response using ACR response, HAQ, DAS28, and physician global scores and plain films.

Results: Both MRI systems were effective in detecting changes in osteitis and erosions. The 1.5T STIR sequence was more sensitive than 0.28T in detecting osteitis. The 0.28T T1W sequence outperformed the 1.5T fat-suppressed T1W sequence in quantifying erosions. Of the 6 pts with osteitis on baseline imaging, scores decreased through 26 weeks in all, and only 1 additional site of osteitis developed. Mean total osteitis score at baseline was 46.5 which increased by 16% to 50 at week 4 due to progression in 3 patients. Osteitis ultimately regressed in all patients and by 26 weeks the mean total osteitis scores had decreased by 78% from baseline to 10.5. Of these patients, 5/6 had significant clinical responses. None of the 4 patients without osteitis at baseline MRI showed any MRI changes during the study; 3 did not achieve an ACR20 clinical response and 1 had a significant ACR response. Erosion scores at 6 sites in 4 patients had regressed by 26 weeks; one new erosion developed. Changes in the mean total erosion scores (76/80/72 at weeks 0/4/26, respectively) were less dramatic than changes seen with osteitis scores. Neither disease duration nor prior use of anti-TNF appeared to have any significant relevance. No x-ray changes were identified during the study. There were no clinically significant adverse effects.

Conclusion: Both low and high field MRI effectively measured the effects and benefits of abatacept treatment during a 26 week period. Patients with baseline osteitis tended to have a more robust clinical and MRI response. Subsequent studies should confirm these findings and better establish the time course of improvements detected by MRI as an outcome measurement and predictor of response to abatacept therapy.

INTRODUCTION

- Low and high field MRI systems have independently been shown to measure erosions and synovitis in rheumatoid arthritis patients. MRI images scored according to RAMRIS criteria^{3,4}.
- Comparative capabilities of low field (0.28T) and high field MRI (1.5T) imaging in rheumatoid arthritis have been published⁵ but not in comparing responsiveness to treatment in an active RA patient.
 - T-cell co-stimulation modulation with abatacept has demonstrated significant response in radiographic progression of patients with early arthritis in the ADJUST Trial⁶.
- In this study, abatacept has been shown to reduce osteitis and erosions in a patient population with high levels of anti-CCP2 antibodies at high risk for developing RA using high field MRI⁷.
- We compared findings of high versus low field MRI on patients with rheumatoid arthritis treated with abatacept over a 6-month follow-up period.

OBJECTIVES

- To explore the comparative capabilities of low (0.28T) versus high field (1.5T) MRI in the detection of changes in wrist and hand findings following treatment with abatacept with methotrexate in rheumatoid arthritis.
- To evaluate the predictive value of MRI in determining if there are findings to suggest patient types who have a higher or lower likelihood to respond to treatment with abatacept and methotrexate.
- To compare MRI findings of high and low field MRI with clinical outcome measurements including ACR score, HAQ score, DAS score, and CRP values.

METHODS

- Ten RA patients who have been unresponsive to either methotrexate alone or in conjunction with an anti-TNF agent with either osteitis or erosions or both on baseline MRI, were treated for 26 weeks with abatacept infusions on day 1, 15, 28, and every 28 days thereafter.
- 0.28T and 1.5T MRI scans of the wrists and hands were obtained at week 0, 4, and 26, and scored by 2 blinded radiologists using OMERACT/RAMRIS systems.
- These results were compared with clinical responses using ACR response, HAQ Scores, Sed Rate, DAS-28, physician global scores, as well as plain films. CCP-2 antibodies and C-reactive protein levels were measured at all intervals.
- The high field sequence used in this study has been published in previous literature⁸.

- Both MRI systems were effective in detecting change in osteitis and erosions.
- The 1.5 STIR sequence was more sensitive than the 0.28T T1W sequence in detecting osteitis.
- The 0.28 T1W sequence outperformed the 1.5 fat suppressed T1W sequence in quantifying erosions.

Figure 1

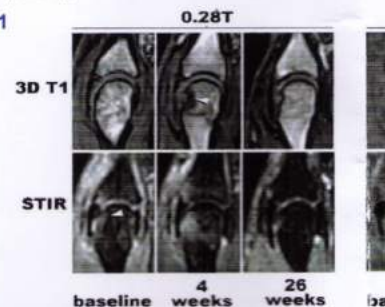


Figure 1 – MRI of the second metacarpal phalangeal joint shows progressive development of a marginal osteitis at baseline and 4 weeks, and resolution of osteitis by 26 weeks. The conspicuous osteitis is more clearly visible on the 0.28T 3D T1 sequence with fat suppression.

Figure 2

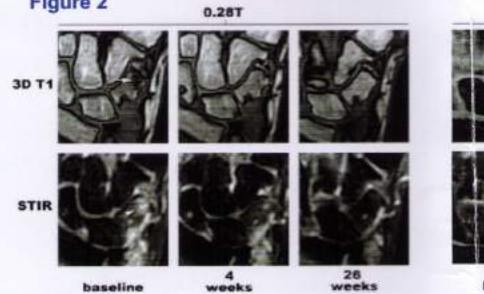


Figure 2 – MRI of the carpus revealed osteitis (arrowheads) in the triquetrum and distal pole of the triquetrum which regressed at 4 weeks. The conspicuity of osteitis was similar on the 0.28T and 1.5T MRI STIR sequences with fat suppression.

- Of the 6 patients with osteitis on baseline imaging, scores decreased through 26 weeks in all, and only 1 additional site of osteitis developed (Figure 1).
- The mean total osteitis score at baseline was 46.5, which increased by 16% to 50 at week 4 due to progression in 3 patients.
- However, osteitis ultimately regressed in all 6 patients and osteitis score had decreased by 78% from baseline to 10.5.
 - Of these patients, 5/6 had significant clinical responses.
 - None of the four patients without osteitis at baseline MRI showed any MRI changes during the study.
 - Three of these patients did not achieve an ACR of 20 clinical response (Table 2).
- Erosion scores of 6 sites in 4 patients had regressed by 26 weeks.
 - Changes in the mean total erosion scores (76, 80 and 72 at weeks 0/4/26, respectively) were less dramatic than changes seen with osteitis scores.
- Neither disease duration nor prior use of anti-TNF therapy appeared to have any significant relevance.
- No significant x-ray changes were identified during the course of the study.
- No correlation between clinical/MRI findings and either CRP or DAS-28 scores.
- No clinically significant adverse events occurred.

Low Field MRI Findings and Clinical Outcomes in Rheumatoid Arthritis Treated With Abatacept

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RESULTS

osteitis and erosions.
 Detecting osteitis (Figure 1).
 STIR sequence when quantifying erosions

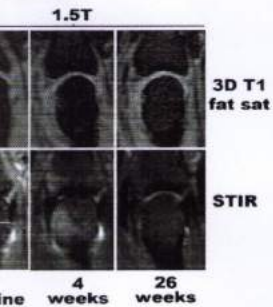


Figure 1: MRI scans showing osteitis (arrowheads) in the metacarpal head between baseline and 4 weeks. The baseline 0.28T 3D T1 sequence showed an erosion (arrow) at 4 weeks which is not easily seen on the 1.5T 3D T1 sequence.

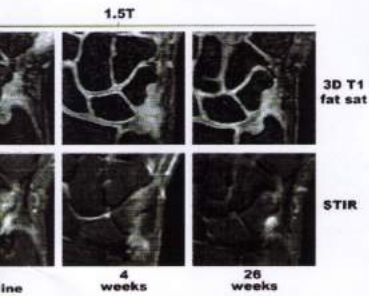


Figure 2: MRI scans showing erosions (arrows) in the metacarpal head between baseline and 26 weeks. The baseline 0.28T 3D T1 sequence showed an erosion (arrow) at 26 weeks which was not well delineated on the 1.5T 3D T1 sequence.

...decreased 26 weeks in all (Table 1); only 1 patient...
 ...decreased by 16% to 50 at week 4 due to...
 ...26 weeks (Figures 1 and 2), the mean total...
 ...showed any MRI changes during the study. The...
 ...total response and 1 had a significant ACR...
 ...weeks. One new erosion developed. (Table 1)...
 ...week 0, 4 and 26 respectively) were less...
 ...appeared to have any significant relevance. The...
 ...of the study. The anti-CCP antibodies was noted.

Table 1

		Baseline	Week 4	6 Months
Patient A	osteitis	1	↑	↓
	erosions	1	no change	↓
Patient B	osteitis	1	↑	↓
	erosions	1	no change	no change
Patient C	osteitis	1	↑	↓
	erosions	1	↑	↓
Patient D	osteitis	0	0	0
	erosions	1	no change	no change
Patient E	osteitis	0	0	0
	erosions	1	no change	no change
Patient F	osteitis	0	0	0
	erosions	1	no change	no change
Patient G	osteitis	0	0	0
	erosions	1	no change	no change
Patient H	osteitis	1	↓	↓
	erosions	1	↓	↓
Patient I	osteitis	1	↓	↓
	erosions	1	no change	no change
Patient J	osteitis	0	0	0
	erosions	1	↑	↓

0=negative 1=positive ↑increased ↓decreased

Table 2

	Baseline	Week 4	6 Months
Patient A			
ACR RESPONSE			50
HAQ	3.0	1.25	0.5
DAS28-ESR	7.75	5.54	2.43
CRP	7.4	1.5	0.4
CCP	32	17	62
Patient B			
ACR RESPONSE			20
HAQ	0.25	0.625	0.875
DAS28-ESR	6.0	3.1	3.88
CRP	0.2	0.3	0.4
CCP	1596	82	20
Patient C			
ACR RESPONSE			20
HAQ	2.12	1.89	2.0
DAS28-ESR	6.67	7.03	6.04
CRP	1.4	1.2	1.8
CCP	956	8	345
Patient D			
ACR RESPONSE			70
HAQ	1.37	1.25	0.125
DAS28-ESR	5.6	4.84	3.34
CRP	0.6	0.0	1.5
CCP	26	108	77
Patient E			
ACR RESPONSE			70
HAQ	1.625	2.0	1.75
DAS28-ESR	6.6	5.06	5.25
CRP	0.7	0.6	1.5
CCP	0	0	2

Table 2 (continued)

	Baseline	Week 4	6 Months
Patient F			
ACR RESPONSE			NR
HAQ	1.25	1.0	1.125
DAS28-ESR	6.67	4.71	5.98
CRP	0.6	0.7	0.7
CCP	0	6	167
Patient G			
ACR RESPONSE			NR
HAQ	0.875	1.25	0.5
DAS28-ESR	6.94	5.07	5.62
CRP	6.1	0.0	1.2
CCP	20	49	94
Patient H			
ACR RESPONSE			70
HAQ	1.25	1.0	0.25
DAS28-ESR	7.13	4.53	3.07
CRP	0.1	1.1	0.6
CCP	56	35	110
Patient I			
ACR RESPONSE			20
HAQ	2.37	1.0	1.5
DAS28-ESR	7.41	4.23	4.58
CRP	0.5	0.7	0.9
CCP	70	73	19
Patient J			
ACR RESPONSE			NR
HAQ	2.0	1.875	1.75
DAS28-ESR	6.41	5.85	7.04
CRP	0.3	0.3	1.9
CCP	160	0	0

CONCLUSIONS

- Both low and high field MRI effectively measured the effects and benefits of abatacept treatment during a 26-week period. Patients with baseline osteitis tended to have a more robust clinical and MRI response.
- It would appear that the response of osteitis to therapy with abatacept may not be noted until 1 month after initiation of therapy. The fact that there was some worsening of osteitis in 3 patients at week 4 possibly suggests either a delayed benefit of abatacept and methotrexate only noticed at 3 months or, alternatively, because of the washout period for these patients.
- Subsequent studies should confirm these findings and better establish the time course of improvements detected by MRI as an outcome measurement and predictor of response to abatacept therapy. The presence of osteitis and response to the therapy appeared in most cases to compare to the clinical outcome measurements.

REFERENCES

- P. Emery, Ann Rheum Dis published online November 23, 2009. doi: 10.1136/ard.2009.119016
- Ejberg B et al, Annual Rheumatic Disease 2005;64(9):1280-1287
- Van Gaalen, FA, et al, Arthritis and Rheumatism, 2004/50, 709-715
- Hetland, M. et al, Annals of Rheumatic Disease 2009/68, 384-390.
- (Bird, P., Ejberg B., Lassere, M., et al. J. Rheum. 2007/34, 854-856)
- Emery, P., et al, Annals of Rheumatic Disease, 2008/67 (suppl II): 89).
- Poterly, Durez, ACR/ARHP, Annual Scientific Meeting, Philadelphia, October 16-21, 2009).

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