

Benefits of Early Onset of DAS28-CRP <2.6 on Physical Functioning, Quality of Life and Resource Use Among RA Patients in a Clinical Practice Setting

E Alemao,¹ S Joo,² H Kawabata,¹ S Banerjee,¹ M Frits,³ C Iannaccone,³ N Shadick,³ M Weinblatt³

¹Bristol-Myers Squibb, Princeton, NJ, USA; ²Bristol-Myers Squibb, Hopewell, NJ, USA; ³Brigham and Women's Hospital, Boston, MA, USA

ABSTRACT

Background/Purpose: Guidelines in RA recommend that treatment should be aimed at reaching a target of remission or low disease activity (LDA) as soon as possible, and that treatment should be adjusted frequently (every 3–6 months) in patients not at target. However, there are limited data from clinical practice on the benefits of attaining rapid remission/LDA. The objective of the current analysis was to compare the clinical and resource use benefits of attaining LDA (DAS28-CRP <2.6) within 1 year in patients with RA in a clinical practice setting.

Methods: Patients enrolled in the Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study (BRASS) Registry, established in 2003, were analyzed. The BRASS Registry mostly comprises patients with established RA who were evaluated semi-annually on multiple clinical patient-reported outcomes and resource utilization parameters. The current analysis is based on the first 5 years of patient follow-up in BRASS and includes patients who were not at DAS28-CRP <2.6 at baseline. Patients attaining DAS28-CRP <2.6 at 1-year follow-up were considered as 'DAS28-CRP <2.6 Soon' and those attaining DAS28-CRP <2.6 later than 1 year were considered as 'DAS28-CRP <2.6 Late'. Clinical (physical functioning measured by modified Health Assessment Questionnaire [mHAQ]), quality of life (QoL; measured by EQ-5D, Short Form [SF]-12 physical component summary [PCS], Patient Health Questionnaire-9 [PHQ-9]), and resource utilization (hospitalization, emergency room [ER] visits, durable medical equipment [DME] use) outcomes up to 5 years were compared in univariate analysis between patients attaining 'DAS28-CRP <2.6 Soon' versus 'DAS28-CRP <2.6 Late'. To control for differences in baseline covariates, generalized linear models were used for continuous outcomes of HAQ, SF-12, EQ-5D and PHQ-9; logit models were used for categorical outcomes of resource use. Covariates in the multivariate analysis included baseline demographics, duration of RA disease, smoking status, baseline disease status, and treatment.

Results: 417 patients with RA were included in the current analysis: 151 (36.2%) were 'DAS28-CRP <2.6 Soon' and 266 (63.8%) were 'DAS28-CRP <2.6 Late'. At baseline, patients in the two groups were similar, respectively, in sex (83 vs 84% females), mean age (SD) (54.2 [12.7] vs 58.3 [13.0] years) and never smoked status (53.0 vs 48.9%). Fewer patients in the 'DAS28-CRP <2.6 Soon' group were on biologic DMARDs than in the 'DAS28-CRP <2.6 Late' group (31.1 vs 38.7%, respectively). Patients in the 'DAS28-CRP <2.6 Soon' group had significantly better mHAQ and QoL, as well as fewer hospitalizations, DME use and ER visits in univariate analysis than the 'DAS28-CRP <2.6 Late' group. Similar findings for all outcomes, except hospitalization/ER visits, were observed in multivariate analysis (see table).

Table. Difference in Outcomes at 1 Year and 2 Years in Patients Attaining DAS28-CRP <2.6 Soon versus Late

Outcomes	1-year post evaluation		2-year post evaluation	
	Mean difference between DAS28-CRP <2.6 Soon vs Late	p-value	Mean difference between DAS28-CRP <2.6 Soon vs Late	p-value
HAQ	-0.127	0.003	-0.097	0.0213
SF-12 PCS	Not available	-	3.84	0.0034
PHQ-9	Not available	-	-1.16	0.0035
EQ-5D	0.057	0.0001	0.036	0.0234
	Odds ratio for DAS28-CRP <2.6 Soon vs Late	95% CI	Odds ratio for DAS28-CRP <2.6 Soon vs Late	95% CI
Hospitalization	0.57	0.29–1.12	0.58	0.24–1.42
DME use	0.55	0.32–0.92	0.49	0.26–0.92
ER	1.17	0.34–4.03	1.52	0.40–5.68

Conclusion: Patients achieving LDA within 1 year benefit more (i.e. more improvement in HAQ and QoL outcomes and lower DME use during follow-up) versus those attaining LDA later. Programs geared towards earlier achievement of guideline targets can improve overall clinical and economic outcomes in RA.

INTRODUCTION

- The current clinical guidelines in RA recommend reaching a target of remission or low disease activity (LDA) as soon as possible, preferably within 3 months.¹
- However, there are limited data from the clinical practice setting on the benefits of attaining rapid remission/LDA.

OBJECTIVE

- To evaluate the clinical and health resource use benefits of attaining LDA, as measured by DAS28-CRP <2.6, soon (next evaluation) versus late in patients with RA in a clinical practice setting.

METHODS

- **Definitions**
 - Patients enrolled in the Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study (BRASS) Registry (established in 2003) were analyzed.
 - The BRASS Registry is comprised of patients with established RA who were evaluated semi-annually on multiple clinical patient-reported outcomes and health resource utilization parameters.
 - The current analysis is based on the first 5 years of patient follow-up in the BRASS Registry and includes patients who were not at DAS28-CRP <2.6 at baseline but reached remission at some point during follow-up. BRASS patients were categorized as 'DAS28-CRP <2.6 Soon' if they did not have a DAS28-CRP <2.6 at baseline but had attained DAS28-CRP <2.6 by Year 1 (earliest point of evaluation in BRASS).
 - Patients in BRASS were categorized as 'DAS28-CRP <2.6 Late' if they did not have a DAS28-CRP <2.6 at baseline and had attained DAS28-CRP <2.6 beyond Year 1.
- Clinical, quality-of-life (QoL) outcomes and resource use were evaluated at Years 2, 3, 4 and 5 by patient groups of 'DAS28-CRP <2.6 Soon' versus 'DAS28-CRP <2.6 Late' as follows:
 - physical functioning: modified Health Assessment Questionnaire (mHAQ)
 - QoL: EuroQoL 5-dimensions questionnaire (EQ-5D), Patient Health Questionnaire-9 (PHQ-9; only for multivariate analysis), Short Form (SF)-12 physical component summary (PCS; only for multivariate analysis)
 - health resource use: hospitalization, emergency room (ER) visits, durable medical equipment (DME) use.

RESULTS

- At baseline, patients in the two groups ('DAS28-CRP <2.6 Soon' vs 'DAS28-CRP <2.6 Late') were similar in sex (83 vs 84% females), mean age (SD) (54.2 [12.7] vs 58.3 [13.0] years) and never smoked status (53.0 vs 48.9%), respectively. Fewer patients in the 'DAS28-CRP <2.6 Soon' group were on biologic DMARDs, steroids, or any type of DMARDs than in the 'DAS28-CRP <2.6 Late' group, but other parameters were similar overall between groups (Table 1).
- 'DAS28-CRP <2.6 Soon' patients had lower mHAQ and higher QoL (EQ-5D and SF-12) scores than 'DAS28-CRP <2.6 Late' patients based on univariate analysis at Years 2, 3, 4 and 5 (Figure 1), and by multivariate analysis at Years 1 and 2 (Table 2).
- Patients who attained 'DAS28-CRP <2.6 Soon' had numerically lower health resource utilization than 'DAS28-CRP <2.6 Late' patients based on univariate analysis at Years 2, 3, 4 and 5 (Figure 2) and significantly lower DME use by multivariate analysis at Years 1 and 2 (Table 3).

Figure 1. RA Patients in the 'DAS28-CRP <2.6 Soon' Group Had Higher QoL and Lower MHAQ scores than 'DAS28-CRP <2.6 Late' Group (Univariate Analysis)

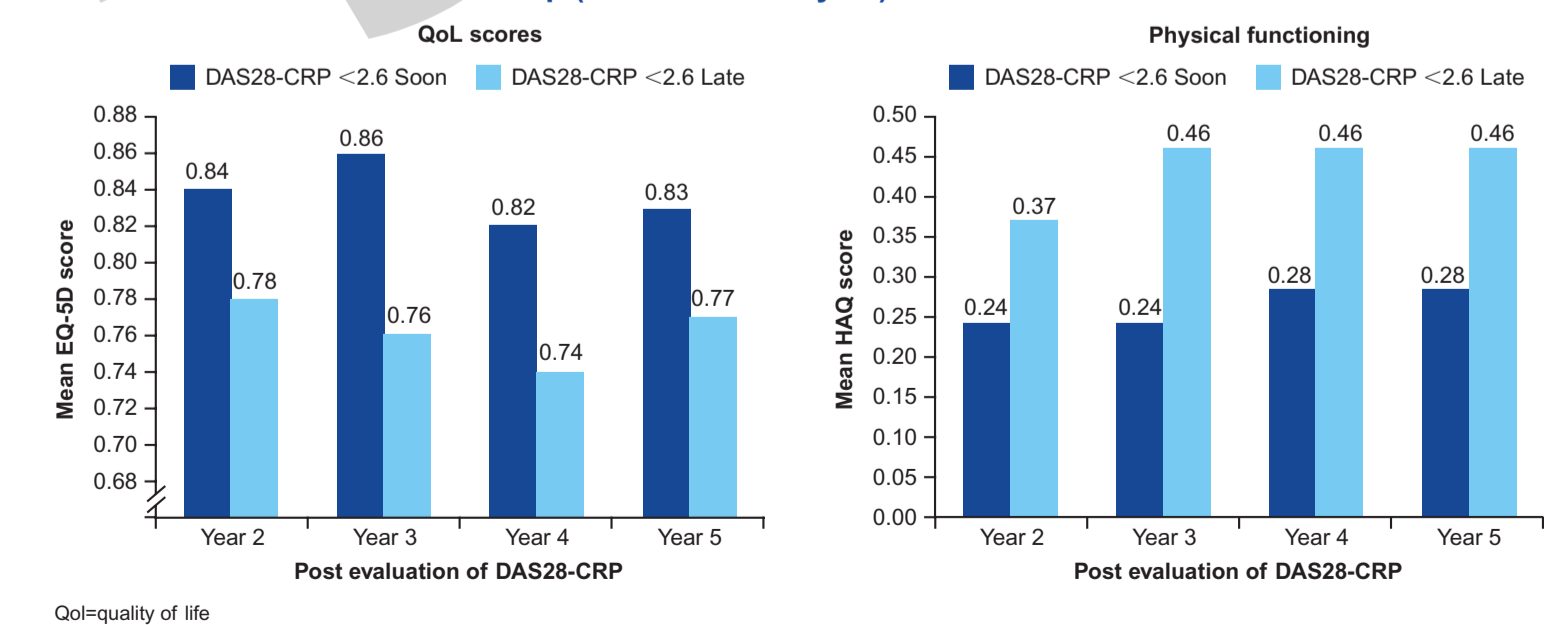


Figure 2. RA Patients in the 'DAS28-CRP <2.6 Soon' Group Had Lower Health Resource Use than 'DAS28-CRP <2.6 Late' Group (Univariate Analysis)

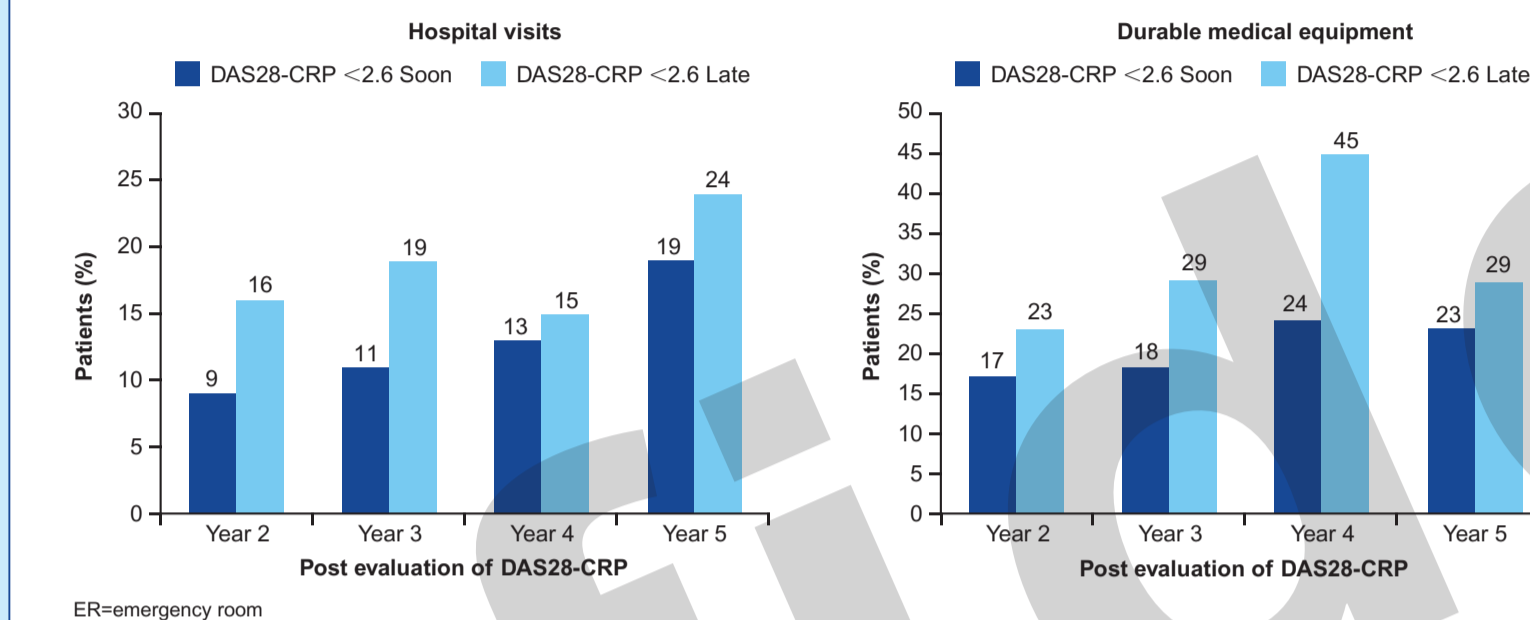


Table 1. Baseline Characteristics of 'DAS28-CRP <2.6 Soon' versus 'DAS28-CRP <2.6 Late' Groups

Characteristic	DAS28-CRP <2.6 Soon (n=151)*	DAS28-CRP <2.6 Late (n=266)*
Female	125 (82.8)	223 (83.8)
Age (years)		
18–39	23 (15.2)	21 (7.9)
40–64	98 (64.9)	155 (58.3)
≥65	30 (19.9)	90 (33.8)
Baseline comorbidities		
0	85 (56.3)	129 (48.5)
1	43 (28.5)	62 (23.3)
2	13 (8.6)	33 (12.4)
≥3	10 (6.6)	42 (15.8)
Smoking status		
Never smoked	80 (53.0)	130 (48.9)
Smoked in the past	49 (32.4)	107 (40.2)
Current smoker	11 (7.3)	14 (5.3)
N/A	11 (7.3)	15 (5.6)
Baseline treatments		
Taking a steroid	33 (21.8)	91 (34.2)
Taking biologic DMARD	47 (31.1)	103 (38.7)
Taking any type of DMARD	125 (82.8)	230 (86.5)
White race	141 (93.4)	245 (92.1)
BMI category (kg/m ²)		
<18.5	1 (0.7)	1 (0.4)
18.5–24.9	59 (39.1)	112 (42.1)
25–29.9	55 (36.4)	75 (28.2)
30–39.9	28 (18.5)	61 (22.9)
≥40	4 (2.6)	6 (2.3)

*Data shown as n (%)

Table 2. Patients with RA in the 'DAS28-CRP <2.6 Soon' Group Had Better Health Function and QoL Outcomes at Years 1 and 2 than the 'DAS28-CRP <2.6 Late' Group (Multivariate Analysis)

Outcome	1st year post-evaluation		2nd year post-evaluation	
	Mean difference between DAS28-CRP <2.6 Soon vs Late	p-value	Mean difference between DAS28-CRP <2.6 Soon vs Late	p-value
mHAQ	-0.127	0.003	-0.097	0.0213
EQ-5D	0.057	0.0001	0.036	0.0234
SF-12 PCS	N/A	-	3.840	0.0034
PHQ-9	-1.160	0.0035	N/A	-

EQ-5D=EuroQoL 5-dimensions questionnaire; N/A=not available; PCS=physical component summary; PHQ-9=Patient Health Questionnaire-9; QoL=quality of life; SF-12=Short Form-12
 MHAQ: n=383 (Year 1) and n=361 (Year 2); EQ-5D: n=382 (Year 1) and n=361 (Year 2); SF-12: n=361 (Year 2); PHQ-9: n=371 (Year 1)

Table 3. Patients with RA in the 'DAS28-CRP <2.6 Soon' Group Had Lower DME Use at Years 1 and 2 than 'DAS28-CRP <2.6 Late' Group (Multivariate Analysis)

Outcome	1st year post-evaluation		2nd year post-evaluation	
	Odds ratio for DAS28-CRP <2.6 Soon vs Late	95% CI	Odds ratio for DAS28-CRP <2.6 Soon vs Late	95% CI
DME use	0.55	0.32–0.92	0.49	0.26–0.92
Hospitalization	0.57	0.29–1.12	0.58	0.24–1.42
ER	1.17	0.34–4.03	1.52	0.40–5.68

DME=durable medical equipment; ER=emergency room visits
 DME: n=392 (Year 1) and n=368 (Year 2); hospitalization: n=339 (Year 1) and n=292 (Year 2); ER: n=184 (Year 1) and n=163 (Year 2)

LIMITATIONS

- Even though there were relatively few imbalances in baseline covariates between groups, this was a retrospective observational analysis and hence associational in nature.
- The DAS28-CRP evaluation was done annually and hence we could not evaluate earlier time points.

CONCLUSION

- Patients achieving DAS28-CRP <2.6 within 1 year tended to benefit more (i.e. greater improvement in physical functioning and QoL outcomes and lower health resource utilization, especially DME use) during follow-up beyond 1 year versus those attaining DAS28-CRP <2.6 later.

REFERENCE

1. Smolen JF, et al. *Ann Rheum Dis* 2014;73:492–509.

ACKNOWLEDGMENTS

This study was sponsored by Bristol-Myers Squibb. Editorial assistance was provided by Paul Wilmott at Caudex Medical and was funded by Bristol-Myers Squibb.

DISCLOSURES

Stock options/bond holdings and employment: Bristol-Myers Squibb. S.J: stock options/bond holdings and employment: Bristol-Myers Squibb. H.K: stock options/bond holdings and employment: Bristol-Myers Squibb. S.B: stock options/bond holdings and employment: Bristol-Myers Squibb. M.F: nothing to disclose. C.I: nothing to disclose. N.S: research grants: AbbVie, Amgen, Genentech; other: BMS, UCB, Crescendo Biosciences. M.W: consulting fees or other remuneration: Bristol-Myers Squibb, Crescendo Bioscience, UCB, Abbvie, Roche, Janssen; research grants: Bristol-Myers Squibb, Crescendo Bioscience, UCB.