Evaluation of Real-World Persistence in Early-Line Abatacept versus Tumor Necrosis Factor Inhibitor in Rheumatoid Arthritis Patients with Anti-Citrullinated Protein Antibody or Rheumatoid Factor Positivity

Poster No. 0249

D Paul,[1] X Han,[1] I Yermilov,[2] SN Gibbs,[2] MS Broder [2]

[1]*Bristol-Myers Squibb, Princeton, NJ, USA;*
[2]*Partnership for Health Analytic Research (PHAR), LLC, Beverly Hills, CA, USA*

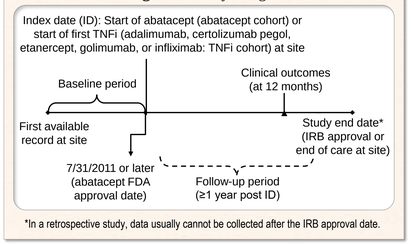
Introduction

- Treatment of active RA usually includes a conventional DMARD, such as methotrexate, sulfasalazine, or leflunomide. Patients who are intolerant or show an inadequate response to conventional DMARDs are often treated with a targeted DMARD.
- There are multiple classes of targeted DMARDs including TNF inhibitors, interleukin-6, CD20, Janus kinase inhibitors, and T-cell co-stimulators such as abatacept.
- In patients with moderately to severely active RA, including patients with positive serologic tests (ACPA+ and/or RF+) who have poorer functional and radiographic outcomes, randomized controlled trials have shown that abatacept inhibits the progression of structural damage, reduces symptoms, and improves physical function.[1]
- However, real-world data on abatacept's use as an early-line biologic agent are limited.

Objective

- The aim of this study was to assess real-world 12-month treatment persistence in early-line abatacept- versus TNFi-treated RA patients who were ACPA+ and/or RF+.

Figure 1. Study design



*In a retrospective study, data usually cannot be collected after the IRB approval date.

Methods

- We performed a multicenter retrospective medical record review of adult RA patients with poor prognostic factors treated at 5 United States clinics located in the West, Midwest, and Southeast.
- Patients were treated with abatacept or TNFi as the first biologic treatment at participating clinics (defined as early line).
- Poor prognostic factors included:[2]
  - Positive anti-cyclic citrullinated peptide antibodies
  - Positive rheumatoid factor antibodies
  - Increased C-reactive protein levels
  - Elevated erythrocyte sedimentation rate levels
  - Presence of joint erosions
- This analysis only included patients who were ACPA+ and/or RF+.
- Patients with Crohn's disease, ankylosing spondylitis, ulcerative colitis, psoriatic arthritis, or anal fistula were excluded.
- TNFis included adalimumab, etanercept, infliximab (and biosimilars), certolizumab pegol, or golimumab.
- Chart data were abstracted into an electronic case report form. Demographic, disease, and treatment data (start, stop, reason for discontinuation) were abstracted. Data were collected from biologic treatment initiation (8/9/11-11/14/16) for ≥12 months (Figure 1).
- Treatment persistence (continuation of index treatment with gap ≤60 days) at 12 months and time to discontinuation were reported.
- Multivariate logistic and Cox regression modeling with forward selection were used to compare 12-month persistence, risk of overall discontinuation, and discontinuation due to disease progression between abatacept and TNFi, controlling for demographic and clinical characteristics (age at index, gender, Charlson comorbidity index (CCI), time from RA diagnosis to index), baseline utilization (number of physician office visits, number of hospitalizations), and clinic.

Results

- Data on 136 patients (47 abatacept, 89 TNFi) were available at the time of analysis (Table 1).
- Abatacept patients were older than TNFi patients. There were no significant differences in gender, CCI, or duration of treatment at the clinic (Table 1).
- Risk of discontinuation was lower in abatacept vs. TNFi patients overall (p=0.029) and for both ACPA+ (p=0.008) and RF+ (p=0.070) patients. Median time to discontinuation for ACPA+ and RF+ patients was 1,672 and 727 days for abatacept vs. 477 and 562 days for TNFi, respectively (Figure 2).
- At 12 months, 83% of abatacept vs. 64% of TNFi patients were persistent (p=0.021) (Table 1).
- Adjusted risk of discontinuation was higher in TNFi patients, although not statistically significant (Table 2).
- Odds of 12-month persistence was lower in TNFi than abatacept patients, but not statistically significant (Table 2).
- Half of TNFi patients (51.85%) discontinued index treatment due to disease progression, compared to 20.00% of abatacept patients (Figure 3). Adjusted analyses showed that TNFi patients had a significantly higher risk of discontinuing index treatment due to disease progression (HR 3.759, p=0.015) (Table 2).

Limitations

- This study included a convenience sample of patients with differing durations of follow-up. Some patients may have follow-up periods that were too short to observe treatment outcomes.
- Off-site care, including imaging studies, procedures, and hospitalizations may not have been thoroughly documented in the patient charts at the study sites.
- Cohorts were compared on an intention-to-treat basis, it is possible that treatment cohorts switched treatment but were evaluated based on their original cohort classification. Patients may also have taken other biologics (either abatacept or TNFi) prior to their index treatment.

Table 1. Baseline characteristics and persistence

	Abatacept (N=47)	TNFi (N=89)	*p*-value
Anti-CCP and RF status			0.075
ACPA+ only	11	11	
RF+ only	17	25	
ACPA+ and RF+	19	53	
Age in years, mean (SD)	64.87 (12.99)	60.48 (11.82)	0.049
Female, n (%)	38 (80.85)	62 (69.66)	0.160
Charlson comorbidity index (CCI), mean (SD)	0.87 (1.17)	0.61 (0.98)	0.182
Duration of treatment at site (years), mean (SD)	5.09 (3.95)	4.74 (3.11)	0.581
Index drug with 12 months of persistence, n (%)	39 (82.98)	57 (64.04)	0.021

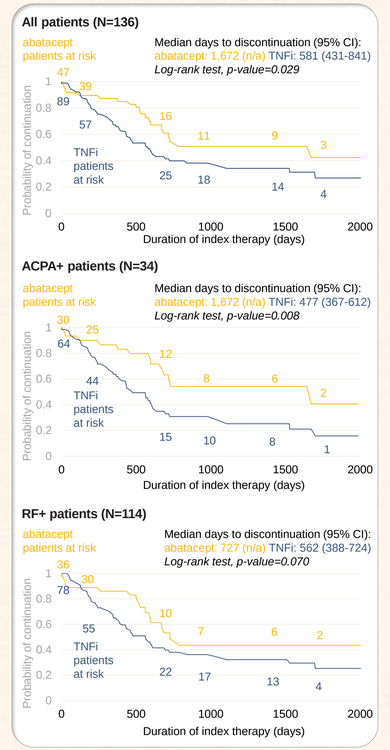
CCI=Charlson comorbidity index; SD=standard deviation

Table 2. Adjusted persistence and risk of discontinuation of index treatment

	Persistence at 12 months: OR (95% CI)	*p*-value	Risk of all-cause discontinuation: HR (95% CI)	*p*-value	Risk of discontinuation due to disease progression: HR (95% CI)	*p*-value
Age, years	1.033 (0.998 - 1.069)	0.064	0.998 (0.979 - 1.017)	0.822	0.988 (0.960 - 1.017)	0.425
Male vs. female	0.254 (0.102 - 0.637)	0.003	1.400 (0.831 - 2.357)	0.206	1.442 (0.663 - 3.136)	0.356
Charlson comorbidity index (CCI)	1.246 (0.802 - 1.934)	0.328	0.995 (0.796 - 1.243)	0.963	1.054 (0.753 - 1.476)	0.758
Anti-CCP and RF status						
Positive anti-CCP only vs. dual positive	2.812 (0.712 - 11.107)	0.140	0.493 (0.228 - 1.069)	0.073	0.337 (0.077 - 1.479)	0.149
Positive RF only vs. dual positive	2.607 (0.996 - 6.826)	0.051	0.495 (0.281 - 0.871)	0.015	0.507 (0.221 - 1.164)	0.109
TNFi vs. abatacept	0.559 (0.217 - 1.439)	0.228	1.525 (0.897 - 2.594)	0.119	3.759 (1.289 -10.966)	0.015

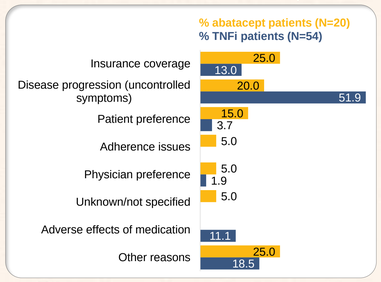
CCI=Charlson comorbidity index; OR=odds ratio; CI=confidence interval; HR=hazard ratio. The initial models included age, gender, CCI, ACPA and RF status, and cohort as independent variables. We then used a forward selection method to include additional significant covariates (p<0.05) in the final models. The following covariates were considered: time from RA diagnosis to index, number of physician office visits (1-year pre-index), number of hospitalizations (1-year pre-index), and clinic site. None of those covariates were significant and therefore were not included.

Figure 2. Time to discontinuation of index treatment



CI=confidence interval

Figure 3. Reason for discontinuation (among patients who discontinued index treatment)



p=0.015
No patients on abatacept reported adverse effects of medication
No patients on TNFis reported adherence issues or unknown/not specified

Conclusions

- In a real-world setting, unadjusted analyses demonstrate that ACPA+ and/or RF+ RA patients are significantly more likely to be persistent to abatacept than TNFi at 12 months.
- Abatacept patients have a longer time to discontinuation than the TNFi cohort. This difference may be explained by the significantly lower proportion of patients discontinuing abatacept due to disease progression.
- Perhaps due to limited sample size, the difference in abatacept and TNFi persistence is not significant, however, numeric trends are consistent.

References

1. Westhovens R, et al. Ann Rheum Dis. 2009;68(12):1870-1877.
2. Emery P, et al. Rheumatol Oxf Engl. 2008;47(4):392-398.

Disclosures

D Paul and X Han are employees of and shareholders in Bristol-Myers Squibb (BMS). I Yermilov, SN Gibbs, and MS Broder are employees of the Partnership for Health Analytic Research (PHAR) LLC, which was paid by Bristol-Myers Squibb to conduct the research described in this poster.

Acknowledgements

This study was sponsored by Bristol-Myers Squibb.