Real-World Evaluation of Persistence with Early-Line Abatacept versus Tumor Necrosis Factor-Inhibitors for Rheumatoid Arthritis Complicated by Poor Prognostic Factors

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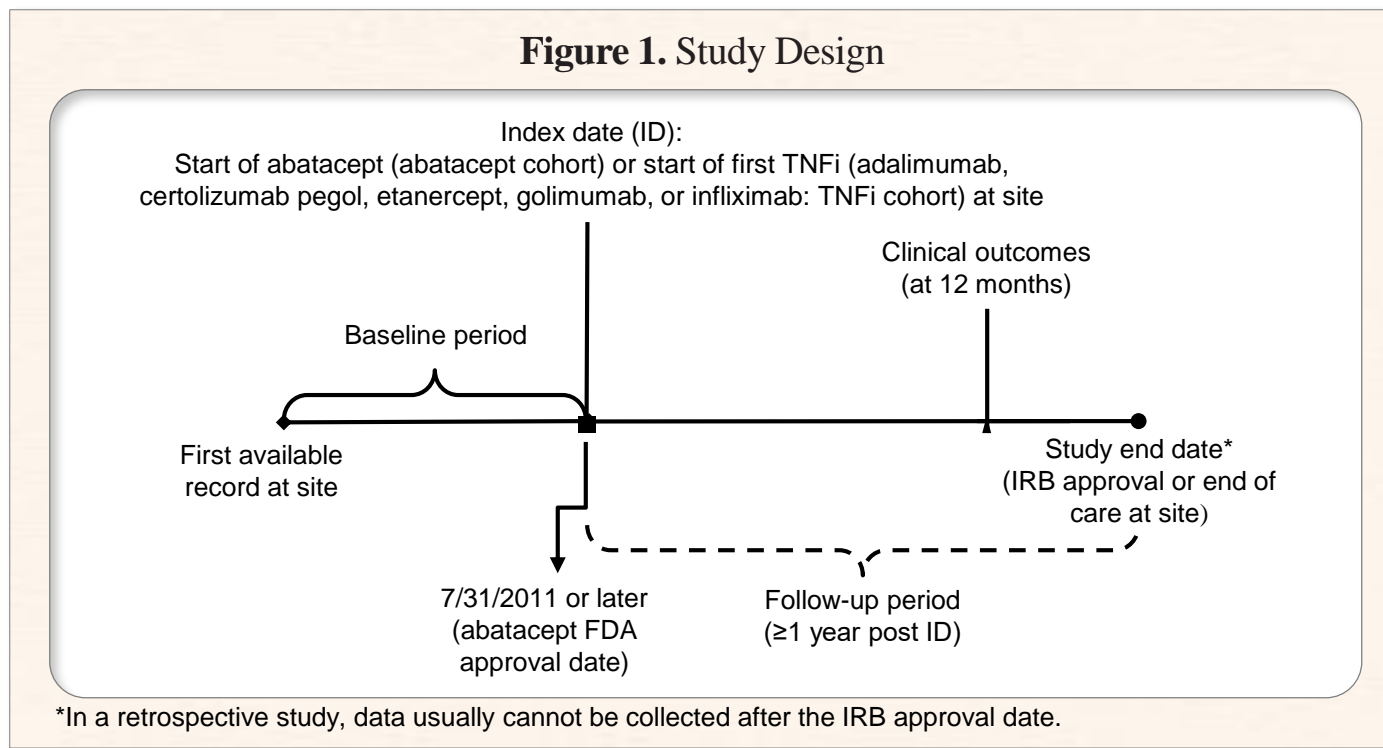*[2]Partnership for Health Analytic Research (PHAR), LLC, Beverly Hills, CA, USA*

Introduction

▶ Treatment of active rheumatoid arthritis (RA) usually includes a conventional disease-modifying anti-rheumatic disease (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 tumor necrosis factor inhibitors (TNFi), interleukin-6 inhibitors, CD20 inhibitors, Janus kinase inhibitors, and T-cell co-stimulators such as abatacept.

▶ In patients with moderately to severely active RA, abatacept inhibits the progression of structural damage, reduces symptoms, and improves physical function.[1] However, the real-world data on abatacept's use as an early-line biologic agent are limited.

▶ This study assessed the 12-month treatment persistence in early-line abatacept versus TNFi treated patients with RA complicated by poor prognostic factors.

Methods

▶ We performed a multicentre 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 the clinic (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

▶ TNFis included adalimumab, etanercept, infliximab (and their biosimilars), certolizumab pegol, or golimumab.

▶ Chart data were abstracted into an electronic case report form. Demographic, disease, and treatment information (start, stop, reason for discontinuation) was abstracted. Data were collected from biologic treatment initiation for ≥1 year. See 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 regressions were used to compare 12-month persistence and overall discontinuation rates between abatacept and TNFi, controlling for demographic and clinical characteristics (age at index, gender, Charlson comorbidity index, time from RA diagnosis to index), baseline utilizations (number of physician office visits, number of hospitalizations), and clinic.

Results

▶ Data on 209 patients (88 abatacept, 121 TNFi) were collected.

▶ Abatacept patients were older than TNFi patients, however there were no significant differences in either gender or duration of treatment at the clinic. See Table 1.

▶ At 12 months, abatacept patients had significantly higher persistence than TNFi patients. Median time to discontinuation was 1,672 days for abatacept versus 612 days for TNFi. See Figure 2.

▶ In the Cox model, the risk of discontinuation was 77% higher in TNFi patients (Hazard Ratio 1.767, 95% Confidence Interval (CI) 1.113-2.806, p=0.0158). See Table 2.

▶ In the logistic regression, the odds of TNFi patients being persistent at 12 months was 52% lower than abatacept, although this difference was not statistically significant (Odds Ratio 0.485, 95% CI 0.208-1.133, p=0.0947). See Table 2.

▶ Reasons for discontinuation differed between cohorts, with more TNFi patients discontinuing due to disease progression and adverse effects of medication. See Table 1.

Figure 1. Study Design

Start of abatacept (abatacept cohort) or start of first TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab: TNFi cohort) at site

Index date (ID):

Clinical outcomes (at 12 months)

Baseline period

First available record at site

Study end date* (IRB approval or end of care at site)

7/31/2011 or later (abatacept FDA approval date)

Follow-up period (≥1 year post ID)

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

References

1. Westhovens R, et al. *Ann Rheum Dis.* 2009;**68**(12):1870–7
2. Emery P, et al. *Rheumatol Oxf Engl.* 2008;**47**(4):392–8.

Table 1. Baseline Characteristics and Persistence

	Abatacept N=88	TNFi N=121	P-Value
Age in years, mean (SD)	64.36 (13.01)	57.23 (13.61)	<0.001
Female, n (%)	70 (79.55)	88 (72.73)	0.257
Charlson comorbidity index, mean (SD)	0.80 (1.07)	0.61 (0.92)	0.178
Duration of treatment at site (years), mean (SD)	5.79 (4.43)	3.67 (4.40)	0.226
Time from index (years), mean (SD)	3.19 (1.52)	3.14 (1.49)	0.808
Index drug with 12 months of persistence, n (%)	76 (86.36)	79 (65.29)	<0.001
Patients who discontinued index treatment any time post-index, n (%)	36 (40.91)	78 (64.46)	<0.001
Reason for discontinuation (among patients who discontinued index treatment), n (%)			<0.001
Disease progression (uncontrolled symptoms or on laboratory testing)	10 (27.78)	42 (53.85)	
Adverse effects of medication	1 (2.78)	9 (11.54)	
Insurance coverage	7 (19.44)	10 (12.82)	
Adherence issues	1 (2.78)	0 (0.0)	
Physician preference	1 (2.78)	0 (0.0)	
Patient preference	2 (5.56)	4 (5.13)	
Unknown/not specified	4 (11.11)	0 (0.0)	

RA=rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor; SD=standard deviation

Table 2. Model Results

	Persistence at 12 months: OR (95% CI)	P-Value	Time to discontinuation: HR (95% CI)	P-Value
Age at index		0.9317		0.6620
Male vs. female	0.538 (0.245-1.184)	0.1235	1.095 (0.709-1.693)	0.6820
Charlson comorbidity index	1.079 (0.751-1.550)	0.6825	0.996 (0.814-1.220)	
Time from RA diagnosis to index (days)	1.000 (1.000-1.000)	0.9779	1.000 (1.000-1.000)	
No. physician office visits (1 year pre-index)	1.006 (0.885-1.144)	0.9227	0.985 (0.915-1.060)	
No. hospitalizations (1year pre-index)	1.246 (0.464-3.348)	0.6622	1.017 (0.559-1.850)	
TNFi vs. Orencia	0.485 (0.208-1.133)	0.0947	1.767 (1.113-2.806)	0.0158
Site		0.0056		0.1296
100 vs. 104	1.771 (0.455-6.887)		0.794 (0.368-1.771)	
101 vs. 104	0.956 (0.284-3.222)		0.856 (0.410-1.786)	
102 vs. 104	8.959 (1.972-40.702)		0.467 (0.221-0.991)	
103 vs. 104	1.992 (0.462-8.583)		0.859 (0.365-2.023)	

RA=rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor; OR=odds ratio; CI=confidence interval; HR=hazard ratio
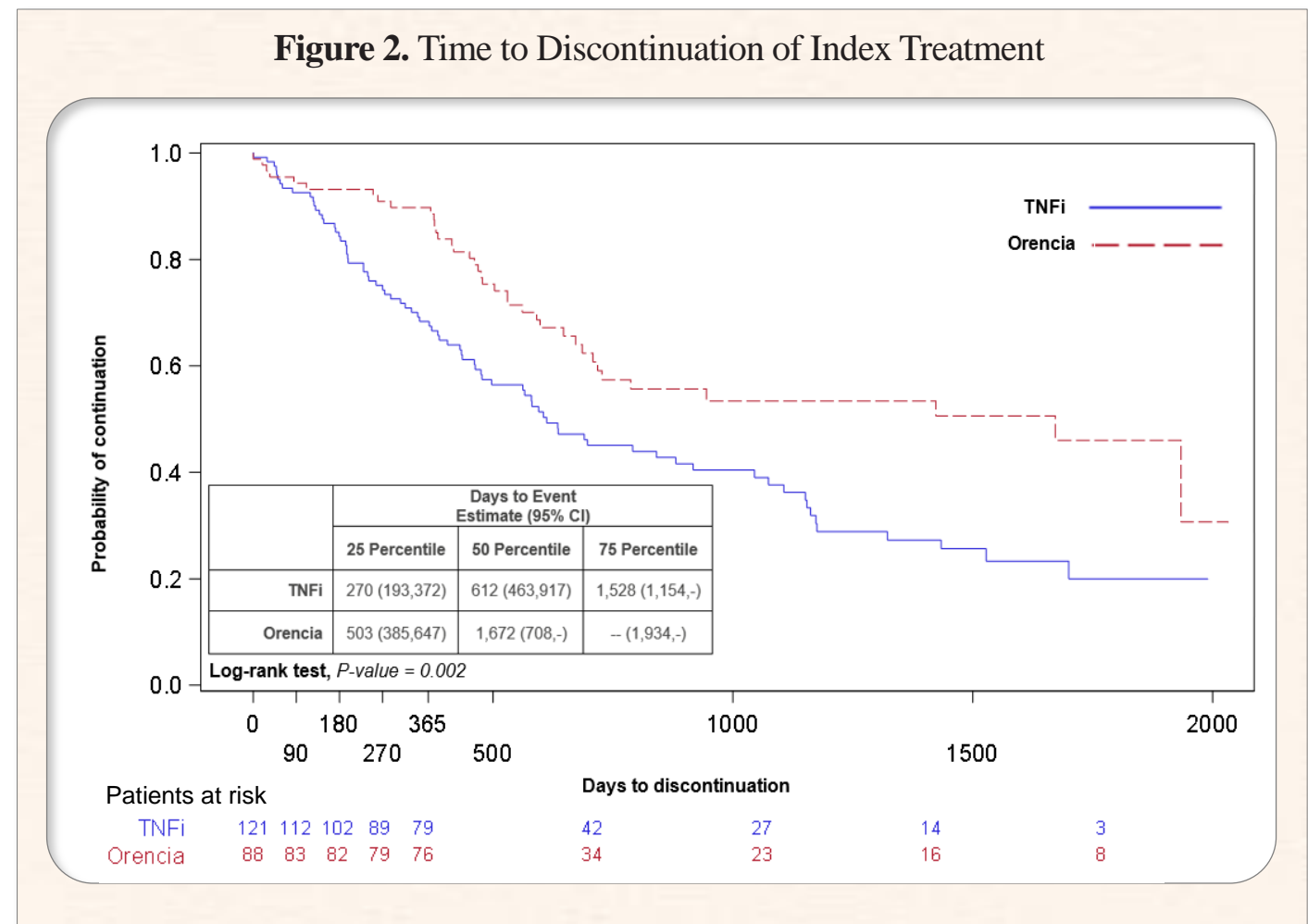
Conclusions

Limitations

▶ There were differences in persistence when stratified by site, which could be related to differences in sample sizes of abatacept and TNFi patients at the sites.

▶ Some patients were treated for RA prior to being treated at the clinic sites. It is possible these patients initiated targeted DMARD therapy at their previous clinic, and the index abatacept or TNFi was not first line therapy.

Conclusions

▶ In a real-world setting, RA patients with poor prognostic factors are significantly less likely to discontinue abatacept than discontinue TNFi.

▶ This difference may be explained by the lower proportion of patients discontinuing abatacept due to disease progression or adverse effects of medication.

Figure 2. Time to Discontinuation of Index Treatment