Effectiveness of new initiators of tofacitinib and other biologic/targeted synthetic DMARDs in patients with rheumatoid arthritis

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Introduction

- Tofacitinib is an oral JAKi for the treatment of RA.
- The efficacy and safety profiles of tofacitinib in RA have been established in previous clinical trials; however, only a limited number of studies have evaluated the effectiveness of tofacitinib compared with bDMARDs in routine care settings.

Objective

- This observational cohort study of patients with RA evaluated the real-world effectiveness of tofacitinib compared with select bDMARDs, both overall and within relevant subgroups of demographic and clinical characteristics.

Methods

Study design

- Data were derived from OM1 PremiOM™ RA (OM1, Boston, MA), a multisource dataset with linked claims and EHR data for patients with RA in the US.
- Patients with RA aged ⩾18 years initiating tofacitinib or select bDMARDs (TNFi [adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab], abatacept, and IL-6i [tocilizumab and sarilumab]) from January 01, 2013–March 13, 2024, who had >1 CDAI score 45 days prior to and including the index date were included.

Statistical analyses

- sIPTW were calculated to adjust for differences in demographics, treatment history, and comorbidities across cohorts.
- Crude IRs per 1,000 PY were calculated to estimate the first record of CDAI remission (⩽2.8) measured at 6 months and 12 months.
- Cox regression with robust standard errors was used to calculate weighted HRs and 95% CIs overall and stratified by baseline CDAI ⩽10 or >10.
- Subgroup analyses by prespecified variables of interest were conducted to assess heterogeneity of treatment effect among patients with baseline CDAI >10.

Results

Patients

- In total, 21,340 patients were included: tofacitinib, N=3,681; TNFi, N=11,667; abatacept, N=3,528; and IL-6i, N=2,464.
- Mean age at index date ranged from 57.9–61.1 years and the proportion of patients with disease duration of ⩾2 years was 48.7–70.0%.
- At baseline, 36.6% of patients initiating tofacitinib had used ⩾2 prior b/tsDMARDs vs TNFi (13.5%), abatacept (31.2%), and IL-6i (49.6%).
- Comorbidities and CDAI scores at baseline were similar between cohorts (**Table 1**).
- After PS weighting, baseline characteristics were well balanced between treatments (all standardized differences <0.1).

Table 1. Demographics/clinical characteristics[a] of patients with RA initiating treatment, before PS weighting

	Tofacitinib (N=3,681)	TNFi (N=11,667)	Abatacept (N=3,528)	IL-6i (N=2,464)
Age at index (years), mean (SD)	57.9 (12.3)	58.1 (13.7)	61.1 (13.1)	60.5 (12.8)
Female, n (%)	2,997 (81.4)	9,171 (78.6)	2,898 (82.1)	1,982 (80.4)
Insurance, n (%)				
Commercial	1,159 (31.5)	3,680 (31.5)	1,165 (33.0)	778 (31.6)
Medicare	1,174 (31.9)	3,884 (33.3)	1,563 (44.3)	1,097 (44.5)
Medicaid	242 (6.6)	617 (5.3)	184 (5.2)	148 (6.0)
Census region, n (%)				
Northeast	514 (14.0)	1,282 (11.0)	389 (11.0)	265 (10.8)
Midwest	466 (12.7)	1,465 (12.6)	366 (10.4)	281 (11.4)
South	2,484 (67.5)	8,155 (69.9)	2,570 (72.8)	1,750 (71.0)
West	211 (5.7)	757 (6.5)	197 (5.6)	165 (6.7)
Disease duration ⩾2 years, n (%)	2,407 (65.4)	5,683 (48.7)	2,185 (61.9)	1,726 (70.0)
Number of previous b/tsDMARD, n (%)				
0	1,087 (29.5)	7,192 (61.6)	1,219 (34.6)	478 (19.4)
1	1,247 (33.9)	2,902 (24.9)	1,209 (34.3)	763 (31.0)
2	787 (21.4)	944 (8.1)	678 (19.2)	627 (25.4)
3	375 (10.2)	350 (3.0)	292 (8.3)	338 (13.7)
⩾4	185 (5.0)	279 (2.4)	130 (3.7)	258 (10.5)
Charlson Comorbidity Index, mean (SD)	2.0 (1.6)	1.9 (1.6)	2.2 (1.7)	2.2 (1.9)
Prior csDMARD use, n (%)	3,113 (84.6)	9,769 (83.7)	2,936 (83.2)	2,018 (81.9)
Baseline corticosteroid use, n (%)	2,414 (65.6)	7,224 (61.9)	2,343 (66.4)	1,720 (69.8)
Baseline obesity (BMI >30 kg/m^2), mean (SD)	30.6 (7.1)	30.5 (7.3)	30.5 (7.3)	30.5 (7.3)
Baseline CDAI score, mean (SD)[b]	19.8 (12.7)	19.1 (12.4)	19.6 (12.5)	20.9 (12.5)
Baseline CDAI score category, n (%)[b]				
Remission: 0.0–2.8	214 (5.8)	741 (6.4)	190 (5.4)	115 (4.7)
Low activity: 2.9–10.0	694 (18.9)	2,298 (19.7)	705 (20.0)	386 (15.7)
Moderate activity: 10.1–22.0	1,457 (39.6)	4,638 (39.8)	1,360 (38.5)	978 (39.7)
High activity: 22.1–76.0	1,316 (35.8)	3,990 (34.2)	1,273 (36.1)	985 (40.0)

TNFi included adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab; IL-6i included tocilizumab and sarilumab

[a]Assessed during the baseline period, defined as all available data prior to and including the index date (date of treatment initiation), unless otherwise stated. For obesity and laboratory measures, the most recent value over the baseline period was used. Patients diagnosed with concomitant indications for tofacitinib (PsA, UC, pcJIA) anytime prior to cohort entry date were excluded (required at least 2 diagnosis codes at least 30 days apart)

[b]Most recent value in the 45 days prior to and including the index date

Treatment switching/discontinuation

- At 6 and 12 months post-index, rates of treatment switching were higher among tofacitinib initiators (5.7–12.9%, depending on treatment comparison) vs comparator treatments (1.7–3.5%), while treatment discontinuation rates were slightly lower among tofacitinib initiators vs comparators (33.8–51.6% vs 36.6–63.0%, respectively).

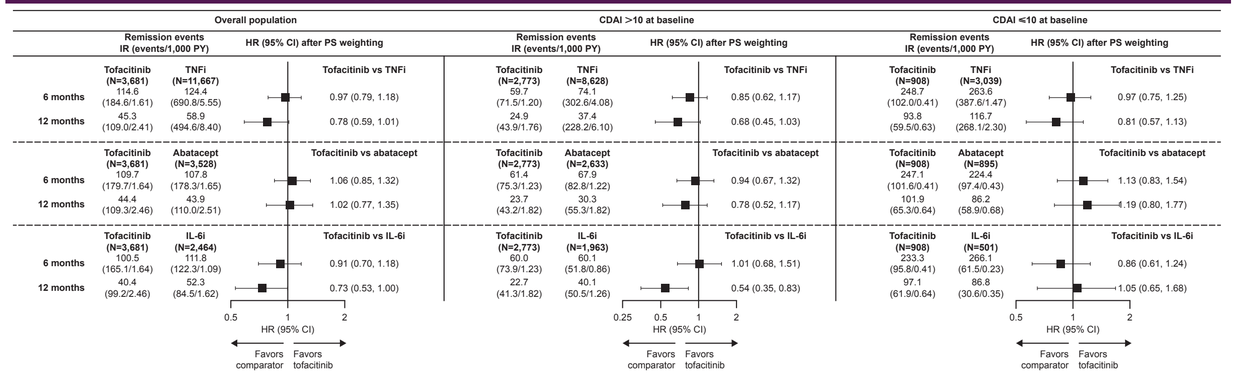
Main analysis

- In the main sIPTW analysis, there were no statistically significant differences in remission rates between treatments at 6 months and 12 months (**Figure 1**).
- Results were consistent when stratifying patients by baseline CDAI ⩽10 or >10, apart from a lower rate of remission for tofacitinib, compared with IL-6i at 12 months among those with baseline CDAI >10 (HR 0.54 [95% CI 0.35, 0.83]).

Subgroup analysis

- Subgroup analyses suggested heterogeneity of treatment effect among patients with obesity (BMI >30 kg/m^2), ⩾2 prior b/tsDMARDs, baseline corticosteroid use, and Sjögren's syndrome for tofacitinib compared with TNFi, among patients with baseline CDAI >10 at 6 months (p-interaction <0.05).
- Heterogeneity of treatment effect was not observed in subgroup analyses at 12 months (p-interaction >0.05; **Figure 2**).

Figure 1. Effectiveness of tofacitinib vs bDMARDs in achieving remission (CDAI ⩽2.8) at 6 months and 12 months



Baseline covariates used to estimate IPTW included: age, sex, race (black, white, other, unknown/not documented), ethnicity (Hispanic, non-Hispanic, unknown/not documented), insurance status (commercial, Medicare, Medicaid, multiple, other, unknown/not documented), census region (Northeast, Midwest, West, South, unknown), BMI (<18.5, 18.5–<25, 25–<30, ⩾30 kg/m^2, unknown), year of index, RA disease duration (<2, ⩾2 years), RA disease activity (CDAI score 0–2.8, 2.9–10, 10.1–22.0, 22.1–76.0), Charlson Comorbidity Index (continuous and categorical: 0–1, 2–3, 4–5, ⩾6), comorbidities (cardiovascular disease, COPD, fibromyalgia, malignancies, osteoporosis, type 1 diabetes, type 2 diabetes, Sjögren's syndrome), smoking status (ever, never, unknown), hospitalization, laboratory results (RF+, RF-, unknown), anti-CCP (positive, negative, unknown), CRP (<3, ⩾3 mg/L, unknown), prior use of medications (csDMARD, bDMARD, tsDMARD), count of prior b/tsDMARDs (0, 1, 2, 3, ⩾4), and corticosteroid use

Conclusions

- **In this large cohort study using real-world data, no significant differences in remission rates were observed between treatments among the overall RA population.**
- **Subgroup analyses suggest some potential heterogeneity of treatment effect for tofacitinib, compared with TNFi; however, interpretation is limited by low event rates, missing data, and potential residual confounding.**

Figure 2. Effectiveness of tofacitinib vs TNFi in achieving remission (CDAI ⩽2.8) at 6 months and 12 months, by subgroup (among patients with CDAI >10 at baseline)

			6 months		12 months	
Subgroup	Tofacitinib (N=2,773)	TNFi (N=8,628)	HR (95% CI) after PS weighting for tofacitinib vs TNFi	p value for interaction	HR (95% CI) after PS weighting for tofacitinib vs TNFi	p value for interaction
Overall	100%	100%	0.85 (0.62, 1.17)		0.68 (0.45, 1.03)	
Age						
⩾65 years	28.0%	32.6%	0.65 (0.38, 1.12)	0.28	0.72 (0.39, 1.32)	0.83
<65 years	72.0%	67.4%	0.94 (0.64, 1.38)		0.66 (0.38, 1.14)	
Age						
⩾50 years	75.8%	74.2%	0.93 (0.65, 1.33)	0.41	0.71 (0.45, 1.12)	0.45
<50 years	24.2%	25.8%	0.66 (0.31, 1.39)		0.48 (0.19, 1.19)	
Sex						
Female	81.6%	79.0%	0.81 (0.55, 1.19)	0.55	0.62 (0.40, 0.95)	0.54
Male	18.4%	21.0%	0.99 (0.57, 1.72)		0.85 (0.34, 2.11)	
RA disease duration						
⩾2 years	64.4%	45.8%	0.77 (0.54, 1.11)	0.54	0.55 (0.33, 0.90)	0.35
<2 years	35.6%	54.2%	0.94 (0.57, 1.54)		0.80 (0.44, 1.47)	
Obesity						
BMI ⩾30 kg/m^2	48.3%	48.6%	1.22 (0.79, 1.90)	0.04	1.00 (0.55, 1.81)	0.08
BMI <30 kg/m^2	50.8%	50.0%	0.62 (0.38, 0.99)		0.43 (0.24, 0.78)	
No. prior b/tsDMARDs						
⩾2	39.1%	13.9%	2.31 (1.10, 4.84)	<0.01	1.15 (0.49, 2.69)	0.24
<2	60.9%	86.1%	0.70 (0.48, 1.01)		0.65 (0.41, 1.02)	
No. prior b/tsDMARDs						
⩾1	72.7%	38.0%	1.18 (0.78, 1.79)	0.09	0.84 (0.54, 1.29)	0.43
0	27.3%	62.0%	0.67 (0.41, 1.11)		0.61 (0.31, 1.18)	
CRP[a]						
⩾3 mg/L	53.1%	52.4%	0.92 (0.59, 1.44)	0.88	0.97 (0.56, 1.70)	0.07
<3 mg/L	25.2%	23.5%	0.81 (0.41, 1.60)		0.23 (0.08, 0.69)	
Baseline steroid use						
Yes	67.6%	64.8%	1.08 (0.73, 1.59)	0.03	0.74 (0.44, 1.26)	0.46
No	32.4%	35.2%	0.51 (0.30, 0.87)		0.55 (0.30, 1.01)	
Smoking status[b]						
Ever	28.3%	25.7%	0.57 (0.31, 1.05)	0.34	0.85 (0.45, 1.61)	0.20
Never	57.4%	58.6%	0.90 (0.60, 1.36)		0.69 (0.39, 1.22)	
Sjögren's syndrome						
Yes	8.2%	6.9%	3.56 (0.95, 13.38)	0.03	0.52 (0.14, 1.88)	0.70
No	91.8%	93.1%	0.78 (0.56, 1.09)		0.68 (0.44, 1.04)	

[a]CRP was unknown in 21.7% (tofacitinib) and 24.2% (TNFi) of patients

[b]Smoking status was unknown in 14.3% (tofacitinib) and 15.8% (TNFi) of patients

Abbreviations

bDMARD, biologic DMARD; **CDAI**, Clinical Disease Activity Index; **CI**, confidence interval; **COPD**, chronic obstructive pulmonary disease; **csDMARD**, conventional synthetic DMARD; **EHR**, electronic health record; **HR**, hazard ratio; **IL-6i**, IL-6 inhibitor; **IR**, incidence rate; **JAKi**, Janus kinase inhibitor; **N**, total number of patients; **n**, number of patients with characteristic; **pcJIA**, polyarticular course JIA; **PS**, propensity score; **PY**, patient-years; **SD**, standard deviation; **sIPTW**, stabilized inverse probability treatment weighting; **SD**, standard deviation; **TNFi**, TNF inhibitor; **tsDMARD**, targeted synthetic DMARD; **UC**, ulcerative colitis.

References

1. DeTora LM et al. Ann Intern Med 2022; 175: 1298–1304.

Acknowledgments

This study was sponsored by Pfizer. Medical writing support, under the direction of the authors, was provided by Lewis C Rodgers, PhD, CMC Connect, a division of IPG Health Medical Communications, and was funded by Pfizer, New York, NY, USA, in accordance with Good Publication Practice (GPP 2022) guidelines.[1]

Disclosure of interests

K Liao has acted as a consultant for Merck. C Gopalakrishnan and S Sarvode Mothi are employees and shareholders of OM1, Inc. J Yazdany has acted as consultant for AstraZeneca and UCB, and has received research grants from AstraZeneca, Aurinia, BMS Foundation, and Gilead. G Gauthier, G Bell, A Yndestad, and M Gianfrancesco are employees and stockholders of Pfizer Inc.

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Poster presented at ACR Convergence, Chicago, IL, USA, October 24–29, 2025