Understanding Patient Preferences Associated with the Use of Therapies for Rheumatoid Arthritis: Results of a Conjoint Analysis

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Abstract

Background and Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Tofacitinib offers a new oral alternative to biologic therapies; however, little is known about the patient preference of modern treatments for RA. Here, we determined patient preferences for attributes associated with therapies used in the treatment of RA.

Methods: A choice-based conjoint survey was mailed to 1400 randomly selected Humana adult members (21-80 years old) diagnosed with RA (continuously enrolled and had ≥2 medical claims with an ICD-9-CM diagnosis code of RA [714.0] between 5/1/2012 and 4/30/2013) and no current or prior use of a biologic indicated for RA. Attributes included route of administration (ROA); monthly out-of-pocket cost, frequency of administration (FOA); ability to reduce daily joint pain and swelling; likelihood of serious side effects (SAE); improvement in the ability to perform daily tasks and activities; and medication burden (methotrexate co-administration). Mean attribute importance scores (AIS) were calculated after adjusting for various member demographics (e.g., age, gender, region, years since RA diagnosis). Mean AIS scores were used to rank order patient preferences for the attributes. An aggregate logit analysis was implemented to estimate average utilities & preference shares for two treatments – a twice daily oral and every other week self- injection.

Results: A total of 380 commercially enrolled members (response rate of 27.1%) in Humana returned the survey (mean ± standard deviation [SD] age 54.9 ± 9.3 years, 9.7% had a history of joint surgery due to RA, 81.6% female). After adjusting for demographic and clinical characteristics, commercial members' ranking of attribute importance was as follows in decreasing order (mean AIS ± SD): ROA 34.1 ± 15.5; FOA 16.4 ± 6.8; SAE 12.0 ± 9.3; cost 10.1 ± 6.2; medication burden 9.8 ± 8.2; joint pain reduction 8.9 ± 3.8; and improvement in daily tasks 8.8 ± 4.7. Within the route of administration attribute, the oral formulation was the level with the highest part-worth utility (preference score) compared with subcutaneous and intravenous routes of administration. Based on the part-worth utility, it was estimated that 56.4% of RA patients included in the sample would prefer oral therapy.

Conclusions: Route of administration is an important consideration for those diagnosed with RA and naïve to biologic therapy. Given the variety of available RA therapies, gaining a better understanding of the attributes considered important to patients in their treatment may help inform payer and prescriber decisions in selecting therapies that could lead to higher patient satisfaction and improved medication adherence.

Background

- Health professionals are increasingly encouraged to involve patients in treatment decisions, recognizing patients as experts who have unique knowledge of their own health.[1-4]
- In order for patient preferences to be effectively used in the delivery of health care, it is important to understand the desire for specific treatment attributes that shape affinities for particular therapeutic products. In the case of Rheumatoid Arthritis (RA), therapies include conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), biologic DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs), including the new therapeutic class of Janus kinase (JAK) inhibitors.[5]
- RA therapies vary in their mechanisms of action; importantly from a patient perspective, they also differ in route of administration. While bDMARDs are administered by infusion or sub-cutaneously, tsDMARDs are administered by mouth. However, little is known about the relative importance of product attributes such as route and frequency of administration.

Objective

The goal of this study was to ascertain relative patient preferences associated with route of administration and other attributes associated with bDMARDs and tsDMARDs in the treatment of RA.

Methods

Study Design: This study involved a cross-sectional survey of patients to ascertain preferences associated with the use of bDMARDs and tsDMARDs for RA.

Study Population

- **Inclusion Criteria:**
  - Currently enrolled in a fully-insured Humana Inc. commercial plan.
  - Age 21 to 80 years old at the time of survey administration.
  - ≥2 diagnoses of RA in the past 12 months at least 30 days apart (ICD9-CM: 714.0).
- **Exclusion Criteria:**
  - Residing in a nursing home.
  - Evidence of a paid claim in claims history for bDMARDs or tsDMARDs indicated for RA, psoriasis, psoriatic arthritis, or ankylosing spondylitis.

Survey Design:

- The survey included 10 choice tasks, and each choice task included two product concepts (Drug A and B), where a product concept was defined by a specific combination of attributes chosen randomly. The conjoint portion was designed with Sawtooth SSI Web software (version 8.2, Sawtooth Software, Inc, Sequim, WA).[6-8]
- 1,400 members were mailed the survey with an anticipated 25% response rate. A four-wave survey roll-out was used and respondents were provided a $10 gift card for their time and effort in completing the survey.

Statistical Analysis:

- Descriptive statistics were used to summarize demographic and clinical characteristics of the study sample obtained from administrative claims data, as well as results of survey questions on prior joint history, length of time with symptoms, and length of time since diagnosis. Two sample t-tests and chi-square tests were used to compare descriptive statistics of respondents to those of non-respondents.
- Conjoint analysis was applied to determine the order of attribute importance. Within Attribute Chi-Squares for main effects and joint effects of the attributes were calculated to determine whether levels of a particular attribute differed significantly in frequency of choice within that respective attribute.
- The influence of demographic and clinical characteristics on each of the attributes was assessed using hierarchical Bayesian estimation, which allows for part-worth utilities calculated at the individual patient level.
- Part-worth utilities were then used to perform conjoint simulations to predict market choice (preference shares) of currently marketed bDMARDs and tsDMARDs.

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Results

Table 1. Descriptive Statistics of Survey Respondents vs. Non-Respondents

Measure	Survey Respondents (n =380)	Survey Non-Respondents (n = 1,020)	*P* value
Age in years, mean (SD)	54.9 (± 9.3)	52.9 (± 10.9)	0.0016
Gender, Female, n(%)	310 (81.6)	795 (77.9)	0.1377
Geographic Region, n (%) , Northeast	1 (0.3)	2 (0.2)	0.0133
Midwest	134 (35.3)	270 (26.5)	
South	229 (60.3)	705 (69.1)	
West	16 (4.2)	43 (4.2)	
RxRiskV comorbidity score, mean [SD]	5.2 (± 2.9)	5.1 (± 3.0)	0.7201
History of Injection/Infusion Utilization, n (%)	136 (35.8)	373 (36.6)	0.7875
Years Diagnosed with Rheumatoid Arthritis, mean (SD)	9.2 (± 9.2)	-	-
Median, Range	6.0 [0.0 - 57.0]	-	-
Years Ago First Experienced Symptoms of Rheumatoid Arthritis, mean (SD)	11.2 (± 10.2)	-	-
Median, Range	8.0 [0.0 - 58.0]	-	-
Joint Surgery Due to Rheumatoid Arthritis, n (%)	37 (9.7)	-	-
Survey Completed by self, n (%)	371 (97.6)	-	-

A total of 380 patients returned the survey, for a response rate of 27.1% (Table 1). A comparison of those that responded to the survey versus those that did not revealed statistically significant differences between the two groups in terms of age and geographic region of residence (both P < 0.05). There were no statistically significant differences between the two groups when comparing gender, RxRiskV comorbidity score, or history of injection/infusion (Table 1).

Table 2. Choice-Based Conjoint (CBC) Analysis of Attributes

Attributes and Levels	Proportion of Times a Concept Containing the Attribute Level was Selected	Within Attribute Chi Square	D.F.*	*P* value
Route of Administration				
By Mouth	0.754	566.57	2	*P* < 0.01
By Self-Injection	0.492			
By Infusion	0.263			
Frequency of Administration				
Twice Daily	0.410	49.77	3	*P* < 0.01
Once Per Week	0.534			
Every Other Week	0.488			
Once Every 8 Weeks	0.567			
Chance of Serious Side Effects				
4 out of 100 people	0.551	43.50	2	*P* < 0.01
6 out of 100 people	0.527			
8 out of 100 people	0.424			
Cost to You				
$25 copay per month	0.573	83.89	2	*P* < 0.01
$50 copay per month	0.536			
$75 copay per month	0.394			
Ability to Reduce Daily Joint Pain and Joint Swelling				
50 out of 100 people	0.519	8.67	3	*P* < 0.05
52 out of 100 people	0.461			
54 out of 100 people	0.497			
58 out of 100 people	0.524			
Improvement in the Ability to Perform Daily Tasks and Activities				
32% improvement	0.500	5.55	3	not sig
33% improvement	0.471			
34% improvement	0.502			
36% improvement	0.527			
Medication Burden (Need to Take with Another Medication)				
No	0.588	110.65	1	*P* < 0.01
Yes	0.412			

*D.F. = Degrees of Freedom.

- Among the respondents, differences in frequency of choice of levels for all attributes were observed, with the exception of "Improvement in Ability to Perform Daily Tasks and Activities" (Table 2). The most frequently selected "Route of Administration" was oral, and once every eight weeks was the most preferred "Frequency of Administration" (Table 2).

Table 3. CBC Utilities and Importance Summary

Attributes and Levels	Average Utility	Standard Deviation	Average Importance	Standard Deviation
Route of Administration				
By Mouth	99.3	72.2	34.1	15.5
By Self-Injection	7.3	57.2		
By Infusion	-106.6	82.8		
Frequency of Administration				
Twice Daily	-51.9	38.9	16.4	6.8
Once Per Week	3.6	22.0		
Every Other Week	3.9	21.5		
Once Every 8 Weeks	43.8	40.6		
Chance of Serious Side Effects				
4 out of 100 people	24.7	47.8	12.0	9.3
6 out of 100 people	6.6	13.6		
8 out of 100 people	-31.4	41.8		
Cost to You (Commercial)				
$25 copay per month	26.1	31.2	10.1	6.2
$50 copay per month	3.4	19.3		
$75 copay per month	-29.5	27.6		
Medication Burden (Take with Another Medication)				
No	29.8	33.0	9.8	8.2
Yes	-29.8	33.0		
Ability to Reduce Daily Joint Pain and Joint Swelling				
50 out of 100 people	-7.5	25.3	8.9	3.8
52 out of 100 people	4.6	23.0		
54 out of 100 people	-6.5	28.1		
58 out of 100 people	9.5	24.3		
Improvement in the Ability to Perform Daily Tasks and Activities				
32% improvement	-4.1	23.7	8.8	4.7
33% improvement	-9.1	26.0		
34% improvement	-0.7	29.4		
36% improvement	13.9	23.5		

A summary of the utilities and attribute importance scores for respondents was generated from the hierarchical Bayes model and reported in Table 3 above. The relative importance of attributes are listed from highest to lowest (Table 3).

Table 4. Assumptions for Base Case and Alternative Case Market Simulations

Base Case Market Simulation				
	Tofacitinib	Adalimumab	Etanercept	Infliximab
Method of Administration	By Mouth	Sub-Cutaneous	Sub-Cutaneous	Infusion
Frequency	2x daily	2 weeks	Weekly	8 weeks
Reduce Joint Pain	54% [a,e]	58% [b,e]	52% [c,e]	50% [d,e]
Improvement in Activities of Daily Living [6]	36%	34%	33%	32%
Serious Adverse Events	4% [a,e]	8% [b,e]	4% [c,e]	6% [d,e]
Medication Burden (take with another medication)	No [a]	No [b]	No [c]	Yes [d]
Member out-of-pocket cost	$65	$65	$65	$65
Alternative Case Market Simulation				
	Tofacitinib	Adalimumab	Etanercept	Infliximab
Method of Administration	By Mouth	Sub-Cutaneous	Sub-Cutaneous	Infusion
Frequency	2x daily	2 weeks	Weekly	8 weeks
Reduce Joint Pain	58%	58%	58%	58%
Improvement in Activities of Daily Living [6]	36%	36%	36%	36%
Serious Adverse Events	8%	8%	8%	8%
Medication Burden (take with another medication)	No [a]	No [b]	No [c]	Yes [d]
Member out-of-pocket cost	$65	$65	$65	$65

a: Pfizer Inc. Xeljanz Prescribing Information. Available at www.xeljanz.com; Accessed 7/21/2014; b: AbbVie Inc. Humira Prescribing Information. Available at www.humira.com; Accessed 7/21/2014; c: Amgen Inc. Enbrel Prescribing Information. Available at www.enbrel.com; Accessed 7/21/2014; d: Janssen Biotech, Inc. Remicade Prescribing Information. Available at www.remicade.com; Accessed 7/21/2014; e: Mapi Values. Efficacy and safety of tofacitinib versus biological treatments for Rheumatoid Arthritis patients who had an inadequate response with DMARDS. Unpublished Pfizer, Inc. internal report P16169D-Version 6. November 4, 2011.

Figure 1. Base Case Market Simulation based on Patient Preferences

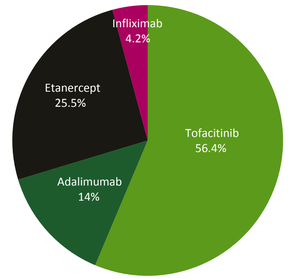
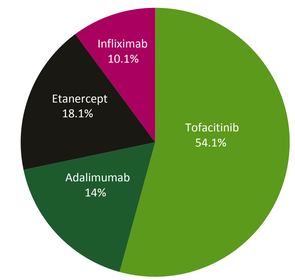


Figure 2. Alternative Case Market Simulation based on Patient Preferences



- Finally, CBC part-worth utilities were used to perform conjoint simulations to predict market choices (preference shares) of currently marketed bDMARDs and tsDMARDs.
- Assumptions for the base case market simulation product concepts are presented in Table 4 (top panel), and results of preference shares reported in Figure 1. Here the product concept with an oral "Method of Administration" and the greatest improvement in "Improvement in Activities of Daily Living" was preferred. Also, the two product concepts with the lowest rates of "Serious Adverse Events" were most preferred.
- Assumptions for the alternative case market simulation product concepts are presented in Table 4 (bottom panel), and results reported in Figure 2. This sensitivity analysis was performed assuming equal efficacy and safety for all product concepts: assuming "Ability to Reduce Joint Pain" was 58% for all product concepts, "Improvement in Activities of Daily Living" was 36% for all product concepts, and "Chance of Serious Adverse Events" was 8% for all product concepts.
- The alternative case market simulation examined the difference in preference share derived solely from "Method of Administration", "Frequency of Administration", and "Medication Burden". Under these conditions, a product taken by mouth, twice daily, and not having to take with another medication was most preferred.

Discussion

- The survey used in this study provided insight into features associated with bDMARDs or tsDMARDs preferred by patients. Among respondents, route of administration (oral) was the most important attribute, followed by frequency of administration (every 8 weeks).
- Interestingly, out-of-pocket cost was not one of the top three attributes of importance among survey respondents. Cost values presented in the study ($25-$75) were fairly consistent with what members currently pay within commercial plans at Humana Inc.(median of $65), which may have influenced the relative importance of the cost attribute.
- Efficacy may have been identified with less frequency since the range of choices was narrower, consistent with the similarity in the reports of efficacy for these compounds in the literature.

Limitations

- Limitations common to studies involving survey methodology apply to this study, including non-response bias. The comparison of respondents to non-respondents indicated significant differences in age and region, but non-significant differences in clinical characteristics examined. It is unknown whether there were significant differences in years since symptoms, years since diagnosis, and history of joint surgery due to RA, potentially adding to non-response bias.
- The survey was quite lengthy; from fatigue or loss of concentration, some individuals may have been at risk of failing to make fully informed and rational choices when answering the survey questions. However, where there was a clear order among levels in an attribute such as cost, the results indicate the appropriate directionality, as expected, for all levels across attributes except for efficacy measures (where levels were quite similar), indicating that individuals were attentive when completing the survey.
- Geographies were not evenly represented.

Conclusions

- **Given the variety of available RA therapies, gaining a better understanding of the features patients prefer most in their treatment may help inform prescriber and payer decisions for selecting therapies that could lead to higher patient satisfaction and improved medication adherence.**
- **Route of administration is an important consideration for those diagnosed with RA and naïve to bDMARD or tsDMARD therapy.**
- **Most RA patients would prefer their therapy have an oral route of administration.**

References **1.** Gonzalez A, Maradit Kremers H, Crowson CS, et al. *Arthritis Rheum.* 2007;56(11):3583-3587. **2.** Myasoedova E, Crowson CS, Kremers HM, et al. *Arthritis Rheum.* 2010;62(6):1576-1582. **3.** Smolen JS, Landewé R, Breedveld FC, et al. *Annals Of The Rheumatic Diseases.* 2014;73(3):492-509. **4.** Palmer D, El Miedany Y. *British Journal of Nursing.* 2013;22(6):308-318. **5.** Smolen JS, van der Heijde D, Machold KP, et al. *Ann Rheum Dis* 2014;73:3-5. **6.** Orme B. *Getting Started with Conjoint Analysis: Strategies for Product Design and Pricing Research.* Madison, WI: Research Publishers, LLC; 2006. **7.** Bridges JFP, Hauber AB, Marshall D, et al. *Value In Health: The Journal Of The International Society For Pharmacoeconomics And Outcomes Research.* 2011;14(4):403-413. **8.** Which Preference Modeling Method Should You Use? 2013; http://www.sawtoothsoftware.com/products/advisor/. Accessed April 24, 2013.

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