Patient Preference and Adherence

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ORIGINAL RESEARCH

Patients' and rheumatologists' preferences for the attributes of biological agents used in the treatment of rheumatic diseases in Spain

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Purpose: To define importance values assigned to attributes of biological agents (BAs) by Spanish patients with rheumatic diseases (rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis) and rheumatologists.

Patients and methods: This was an observational, cross-sectional design based upon a rank-based full-profile conjoint analysis. A literature review and four focus groups were undertaken to identify attributes and levels. An orthogonal matrix, combining the selected levels of attributes, was used to define scenarios. Participants ranked eight scenarios from 1 (most preferred) to 8 (least preferred). The relative importance (RI) of attributes was calculated. Multivariate regression analysis was performed to identify the characteristics that influenced the values of RI. A total of 488 patients (male 50.9%, mean age 50.6 [standard deviation {SD} 12.06] years, rheumatoid arthritis 33.8%, ankylosing spondylitis 32.4%, psoriatic arthritis 33.8%; mean time since diagnosis 12.6 [SD 8.2] years) and 136 rheumatologists (male 50.4%, mean age 46.4 [SD 9.1] years, mean time of practice 16.7 [SD 8.8] years) participated.

Results: The ideal BAs for patients and physicians, respectively, should allow pain relief and improvement of functional capacity (RI 39% and 44.7%), with low risk of adverse events (RI 24.9% and 30.5%), a long time prior to perceiving the need for a new dose (RI 16.4% and 12.4%), and self-administration at home (RI 19.7% and 12.5%), as identified through their preferences.

Conclusion: Although efficacy and safety are paramount for patients and rheumatologists to make a choice regarding BAs, the need for a low frequency of administration and the administration method also play a role as preference attributes for BAs.

Keywords: preferences, conjoint analysis, attributes, biological agents, rheumatic diseases

Introduction

Rheumatic diseases (RDs) represent a multitude of chronic degenerative, inflammatory, and autoimmune conditions affecting millions of people worldwide.[1] In Spain, the prevalence of RD can reach 23%.[2] Three of the most prevalent RDs are rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA).[3–6] All three pathologies are characterized by their potential to cause disability,[7] their negative influence on patients' quality of life (QoL)[8] and functional capacity, and by the immense consumption of health care resources and loss of productivity they entail.[9]

Traditional treatment of inflammatory RDs includes the use of symptom-modifying therapies (nonsteroidal anti-inflammatory drugs and corticosteroids), combined with nonbiologic disease-modifying antirheumatic drugs (DMARDs).[10,11] The development of new biological therapies, particularly TNF inhibitors, has led to significant improvement in clinical outcomes, including symptoms, health-related QoL (HRQoL),

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and functioning.[12] However, this scenario is associated with a more complex decision-making process. These newer therapies present different routes of administration, increased or different toxicities, and higher financial costs, all of which may influence patient preferences and adherence to medications.[13]

Assessing and including patient preferences within routine clinical practice has been related to an increment in medication adherence, improvements in treatment outcomes, and reduced health care costs.[13–19] Since the first studies that examined patient preferences for biological agents (BAs) in RA were published,[20,21] rheumatologists have started to use patient-focused outcomes to improve RA treatment.[22] Nevertheless, it is possible that RD outcomes could be improved further if rheumatologists were aware of how patients used and perceived newer medications,[23] thereby reinforcing the importance of understanding patients' attitudes toward treatment and involving them in shared decision making.[13] The aim of this study was to define the importance values (preferences) assigned to the attributes of BAs by Spanish patients with the main RDs – RA, AS, and PsA – and by their rheumatologists.

Materials and methods

Design

An observational cross-sectional study was conducted in 41 Spanish hospitals, based on a conjoint analysis methodology. The conjoint analysis method is particularly useful for quantifying preferences for a diverse range of health applications. It consists of a composition method, in which the implicit values for an attribute of an intervention are derived from the overall score for a profile consisting conjointly of two or more attributes.[24] It is also used to understand patient preferences for health states, to value the various health states described by patient-reported outcomes and HRQoL scales,[25] and to assess patients' willingness to accept the therapeutic risks associated with more effective treatments.[24] Conjoint analysis also offers a mechanism for patients to participate in the decision-making process.[26,27]

The conjoint analysis technique uses questionnaire data. In the present study, a rank-based full-profile conjoint was applied. In this method, individuals are first presented with, and then asked to give an ordinal ranking to the options of hypothetical scenarios involving different levels of characteristics, which have been identified as important to the question of interest.[28] Those options that achieve the highest ranking are viewed as the most important. Since it is considered easy to answer and to analyze, this method has become popular for eliciting preferences for health care interventions.[29]

Following the International Society For Pharmacoeconomics and Outcomes Research good research practices for conjoint analysis,[24] a literature review was performed to identify the preliminary set of attributes and levels of BAs most frequently described in publications. Subsequently, a focus group with rheumatologists (n=5) and three focus groups with patients (n=5) – one for each pathology (RA, AS, and PsA) – were formed. Focus groups helped define, from the identified attributes, the final set of attributes and levels included in the study, reflecting both patients' and professionals' perspectives regarding BAs.

Table 1 shows the four attributes of BAs included in the study, with their respective levels: administration method (subcutaneous self-administration at home, intravenous administration by a health care professional at hospital), risk of adverse events (AEs; high risk of AEs, low risk of AEs), pain relief (pain relief and improvement in functional capacity, no pain relief and no improvement in functional capacity), and duration of effect (1 week, 2 weeks, 4 weeks, 8 weeks).

For definition of the scenarios, an orthogonal design was used. A full-choice fractional factorial design was implemented using SPSS version 19.0. This orthogonal design, combining the levels of the attributes, resulted in eight scenarios, which described different alternatives of treatment with BAs for RA, AS, or PsA.[30]

A self-completion hard-copy case-report form (CRF) was specifically designed to collect data from participants.[31] Patient CRFs included sociodemographic (age, sex, marital status, place of residence, level of studies, employment status, and other variables) and clinical variables (height, weight, date of onset of first symptoms, diagnosed rheumatic illness, date

Table 1 Attributes and levels included in the scenarios

Attribute	Level
Administration method	• Subcutaneous self-administration at home • Intravenous administration by a health care professional at hospital
Risk of adverse events	• High risk of adverse events • Low risk of adverse events
Pain relief and improvement in functional capacity	• Pain relief and improvement in functional capacity • No pain relief and no improvement in functional capacity
Duration of effect (time until perceiving the need for a new dose)	• 1 week • 2 weeks • 4 weeks • 8 weeks

of diagnosis, disabling symptoms and complications associated with RD, comorbidities, current treatment, and previous treatment), as well as participants' preferences. In patient CRFs, clinical and sociodemographic data were collected by rheumatologists taking part in the study during routine practice, while patients ranked the scenarios from 1 (most preferred) to 8 (least preferred). In addition, professionals self-completed another CRF based on their sociodemographic data (age, sex, work center, time of professional experience) and preferences. Professionals ranked the scenarios from 1 (most preferred to prescribe) to 8 (least preferred to prescribe). Missing data for variables are presented in Table 2.

Participants

The study protocol was approved by the ethics Committee of the Bellvitge Hospital Universitari (Acta 01/13, reference EPA047/12). All participants in the study provided written consent. A total of 41 hospitals in the public health sector where BAs for RDs were prescribed were purposefully identified around the country, covering the whole Spanish territory. A rheumatologist at each selected hospital was required to recruit a minimum of four to five ambulatory patients for each condition under study (n=12–15), as well as a minimum number of rheumatologists (three to four) working in the same or a similar health care centre.

Table 2 Patient sociodemographic and clinical variables

Patient variables	Total (488)	RA (165)	AS (158)	PsA (165)	*P*-value
Age (years), mean (SD)	50.61 (12.06)	55.9 (11.5)	46.3 (11.4)	49.5 (11.4)	<0.001
Sex					<0.001
Male (%)	50.9	26.2	71.8	55.8	
Female (%)	49.1	73.8	28.2	44.2	
	MD 0.6%	MD 0.6%	MD 1.3%	MD 0	
Marital status					0.016
Married (%)	70.1	72.1	63.3	74.5	
Single (%)	14.8	10.3	22.8	11.5	
Cohabiting (%)	6.4	5.4	7.6	6.1	
Separated/divorced (%)	4.9	5.4	5.1	4.3	
Widowed (%)	3.9	6.7	1.2	3.6	
Place of residence					0.136
Living at own home (%)	92.2	95.7	87.9	92.7	
Living at parents' home (%)	5.8	2.4	9.6	5.5	
Living at home of others (%)	1.9	1.8	1.9	1.8	
	MD 0.4%	MD 0.6%	MD 0.6%	MD 0	
Level of studies					0.413
Primary (%)	35.2	39.4	29.1	36.9	
Secondary (%)	24.8	18.8	20.2	15.2	
Other (%)	40	42.2	50.7	47.9	
Employment status					<0.001
Employed (%)	38.6	25.9	45.8	44.2	
Sick leave due to RD (%)	13	16.6	11.6	10.9	
Retired (%)	16.4	25.9	6.5	16.4	
Other (%)	32	32.7	36.6	28.5	
Other variables					
Regular alcohol consumption (%)	16	11.7	22.1	14.6	0.034
	MD 1.4%	MD 1.2%	MD 2.5%	MD 0.6%	
Nonsmokers (%)	49.1	53.0	47.5	46.7	0.098
Weight (kg), mean (SD)	75.8 (15.4)	71.1 (14.9)	77.6 (15.3)	78.6 (15)	<0.001
	MD 0.8%	MD 1.2%	MD 0	MD 1.2%	
Height (cm), mean (SD)	166.5 (9.3)	162.7 (8.7)	169.3 (8.9)	167.4 (9)	<0.001
	MD 0.8%	MD 1.2%	MD 0	MD 1.2%	
BMI (kg/m^2), mean (SD)	27.3 (4.8)	26.8 (5)	27 (4.6)	28 (4.9)	0.058
	MD 0.8%	MD 1.2%	MD 0	MD 1.2%	
Charlson index, median (SD)	0.4 (0.7)	0.5 (0.8)	0.2 (0.6)	0.3 (0.7)	<0.001
	MD 0.4%	MD 0.6%	MD 0	MD 0.6%	
Time since first symptoms, mean (SD)	15 (9.6)	14.1 (8.5)	17.4 (11.2)	13.6 (8.5)	0.005
Time since diagnosis (years), mean (SD)	12.6 (8.2)	13 (7.8)	13.1 (9.2)	12.6 (8.2)	0.142

(*Continued*)

Table 2 (*Continued*)

Patient variables	Total (488)	RA (165)	AS (158)	PsA (165)	*P*-value
Disabling symptoms					
None	29.1%	25.5%	30.4%	31.5%	0.437
Joint rigidity	30.9%	25.5%	8.2%	18.2%	0.759
Joint swelling	17.4%	30.9%	32.9%	29.1%	<0.001
Joint pain	51.8%	58.8%	43.7%	52.7%	0.055
	MD 0.2%				
Limitation of functional capacity	34%	37.6%	39.2%	25.5%	0.016
Others	4.3%	3.6%	7.6%	1.8%	0.033
Complications associated with RD					
Without complications	68.9%	22.7%	20.9%	25.2%	0.132
Amyloidosis	0.4%	0	0.2%	0.2%	0.598
Anemia	2.7%	1.8%	0.4%	0.4%	0.05
	MD 0.2%				
Cardiac complications	1.4%	1%	0	0.4%	0.07
Intestinal complications	3.5%	0.6%	2.3%	0.6%	0.015
Ocular complications	10%	2.9%	5.9%	1.2%	<0.001
Renal complications	1.2%	0.4%	0.4%	0.4%	0.999
Pulmonary complications	2.7%	2.3%	0.2%	0.2%	0.001
Neurological complications	0.8%	0.2%	0.4%	0.2%	0.751
Others	9.8%	3.7%	2.0%	4.1%	0.185
Comorbid conditions					
Without comorbidities	43.9%	12.7%	16.2%	15%	0.078
	MD 0.2%				
Infectious and parasitic	2%	1%	0.4%	0.6%	0.519
	MD 0.2%				
Neoplasia	0.8%	0.8%	0	0	0.043
	MD 0.4%				
Endocrine, nutritional and metabolic	22.7%	10.5%	4.7%	7.6%	0.002
	MD 0.2%				
Blood and hematopoietic organs	1.6%	0.2%	0.6%	0.8%	0.406
	MD 0.2%				
Mental disorders	1.6%	0.2%	0.8%	0.6%	0.386
	MD 0.2%				
Nervous system and sense organs	1.8%	1%	0.6%	0.2%	0.33
	MD 0.4%				
Circulatory system	12.7%	5.9%	2.9%	3.9%	0.055
	MD 0.2%				
Respiratory system	4.1%	1.4%	1.4%	1.2%	0.935
	MD 0.2%				
Digestive system	7%	1.6%	3.3%	2%	0.153
	MD 0.2%				
Genitourinary system	4.1%	1.2%	1%	1.8%	0.537
	MD 0.2%				
Skin and subcutaneous tissue	3.5%	0.4%	1.2%	1.8%	0.104
	MD 0.2%				
Osteomyoarticular system and connective tissue	6.4%	3.1%	1.2%	2%	0.148
	MD 0.2%				
Congenital anomalies	0.2%	0.2%	0	0	0.376
	MD 0.2%				
Others	8.8%	2.3%	2.3%	4.3%	0.09
	MD 0.4%				

Note: Percentages calculated on data available.

Abbreviations: MD, missing data; BMI, body mass index; RA, rheumatoid arthritis; AS, ankylosing spondylitis; PsA, psoriatic arthritis; SD, standard deviation; RD, rheumatic disease.

Patients' inclusion criteria included having been diagnosed with RA, AS, or PsA at least 2 years prior to their inclusion and currently or previously (≤1 year ago) receiving BAs for a minimum of 1 year. Exclusion criteria included a need to translate questionnaire, coexistence of the studied RDs, incapacity to participate due to clinical, physical, or intellectual factors according to clinician judgment, and currently taking part in a clinical trial. Rheumatologists were required to have at least 3 years' experience in the use of BAs, and were excluded if they practiced only in the private sector.

Statistical analysis

A descriptive statistical analysis was performed for sociodemographic, clinical, and treatment variables. A rank-ordered logit model was applied to estimate the preferences or partial utilities of each attribute, which indicated the perceived value of the feature. The relative importance (RI) of attributes was calculated from these partial utilities (the utility ranges of an attribute divided by the sum of the ranks of the four attributes of each individual), allowing the comparison of values between the two groups. To identify the clinical and sociodemographic characteristics that influenced the value of RI given to each attribute by both patients and rheumatologists, a multiple-regression analysis was performed where the values of importance were considered dependent and the clinical and sociodemographic variables independent variables. All variables were included in the analysis, but to reduce the number of independent variables and to avoid problems of collinearity, a stepwise algorithm was implemented. The software SPSS version 19.0 was used for all statistical tests, and a significance level of $P<0.05$ was assumed. To compare the values obtained in the different groups, the χ^2 test was performed for qualitative variables. Parametric distributions were analyzed with analysis of variance, while nonparametric distributions were examined with the Kruskal–Wallis test.

Results

Descriptive analysis

A total of 488 patients were included, distributed equally among diseases (RA 33.8%, AS 32.4%, and PsA 33.8%). The sample mean age was 50.61 (standard deviation [SD] 12.06) years. In the RA sample, 73.8% were females, while in the AS and PsA groups, males accounted for 71.8% and 55.8%, respectively (Table 2).

Average sample weight and height were 75.8 kg and 166.5 cm, respectively, with significant differences between diseases. The mean Charlson index score was 0.4 (SD 0.7), with significant differences (P=0.001) among pathologies (RA 0.5 [SD 0.8], AS 0.2 [SD 0.6], and PsA 0.3 [SD 0.7]). At inclusion in the study, the mean time since the diagnosis of the RDs was 12.6 (SD 8.2) years, while the mean time since the onset of symptoms was 15 (SD 9.6) years. The most common disabling symptoms reported were joint pain (SD 51.8%) and limitation of functional capacity (34%) (Table 2). The sample mean body mass index was 27.3 kg/m^2 (SD 4.8), and 43.9% of the population studied did not present comorbidities (secondary diagnoses). According to physician judgment, most of the patients did not have complications associated with their RD (68.9%), considered as an unfavorable evolution of the disease. The complications taken into account were amyloidosis, anemia, cardiac, intestinal, ocular, renal, lung, and neurological complications, and others, but only ocular (10%), intestinal (3.5%), and pulmonary (2.7%) complications showed significant differences between pathologies (Table 2). Of comorbidities reported, the most common were endocrine, nutritional, and metabolic conditions (22.7%), and these, together with neoplasia, were the comorbid conditions with marked differences between pathologies.

Table 3 shows the BAs most frequently received by patients – mainly etanercept (27.3%), adalimumab (26.2%),

Table 3 Number and percentage of patients receiving treatment with BAs at the time of study inclusion, and previous treatment

	Actual treatment with BAs				Previous treatment with BAs			
	Total, %	RA	AS	PsA	Total, %	RA	AS	PsA
Etanercept	133 27.3%	23.6%	20.9%	37%	44 9%	12.7%	6.3%	7.9%
Adalimumab	128 27.3%	21.2%	27.2%	30.3%	52 10.7%	14.5%	12%	5.5%
Infliximab	113 23.2%	9.7%	36.7%	23.6%	46 9.4%	8.5%	10.1%	9.7%
Golimumab	37 7.6%	2.4%	13.3%	7.3%	13 2.7%	3%	1.9%	3%
Tocilizumab	25 5.1%	15.2%	0	0	4 0.8%	2.4%	0	0
Abatacept	24 4.9%	12.1%	0.6%	1.8%	2 0.4%	1.2%	0	0
Rituximab	12 2.5%	7.3%	0	0	4 0.8%	2.4%	0	0
Certolizumab pegol	9 1.8%	5.5%	0	0	2 0.4%	1.2%	0	0
Ustekinumab	1 0.2%	0	0	0.6%	0	0	0	0

Abbreviations: BAs, biological agents; RA, rheumatoid arthritis; AS, ankylosing spondylitis; PsA, psoriatic arthritis.

and infliximab (23.2%) – with the mean duration of treatment being 49.7 (SD 36.7) months, as well as those BAs previously received – mainly adalimumab (10.7%), infliximab (9.4%), and etanercept (9%) – with an average duration of 43.8 (SD 37.5) months. With regard to rheumatologists, the sample consisted of 136 participants: 50.4% males with a mean age of 46.4 (SD 9.1) years. The mean time of professional experience was 16.7 (SD 8.8) years.

Preferences for BA attributes

The conjoint analysis models proved to fit: Pearson's R=0.991 (P<0.001) and Kendall's τ=0.929 (P<0.001) for patients, and Pearson's R=0.996 (P<0.001) and Kendall's τ=1 (P<0.001) for rheumatologists. Figure 1 demonstrates that each attributes' preferred levels for both patients and rheumatologists were similar: subcutaneous self-administration at home (utility values 0.26 and 0.37), low risk of AEs (utility values 0.81 and 1.03), pain relief and improvement of functional capacity (utility values 1.26 and 1.59), and duration of effect (time until perceiving the need for a new dose) of 8 weeks (utility values 0.53 and 0.61), respectively.

Figure 2 shows the RI given by both patients and rheumatologists to the attributes of BAs and for specific rheumatic conditions. Based on the utility values calculated by the model, both patients, with independence of the diagnosis, and physicians placed more importance on the pain relief and improvement in functional capacity attribute (RI 39% and 44.7%), followed by the risk of AEs (RI 24.9% and 30.5%), administration method (RI 19.7% and 12.5%), and duration of effect (time until perceiving the need for a new dose) (RI 16.4% and 12.4%), respectively. However, significant differences (P<0.002) were found on the RI given to the four attribute values by both groups of participants. Patients placed higher importance on the administration method and duration of effect (time until perceiving the need for a new dose) attributes, compared to rheumatologists, while the latter gave more importance to pain relief, improvement in functional capacity, and risk of AEs, than patients did.

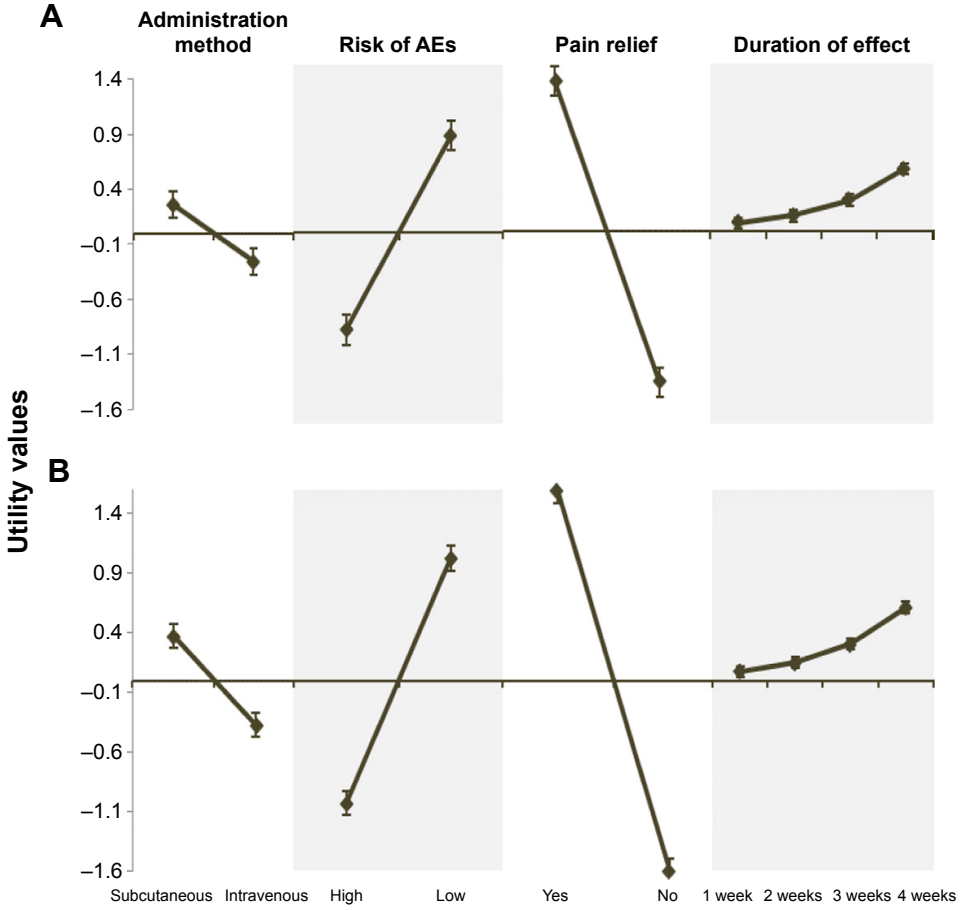

Figure 1 Patients' (**A**) and rheumatologists' (**B**) utility values.
Note: Estimated utility values for each attribute in the sample of patients and rheumatologists.
Abbreviation: AEs, adverse events.

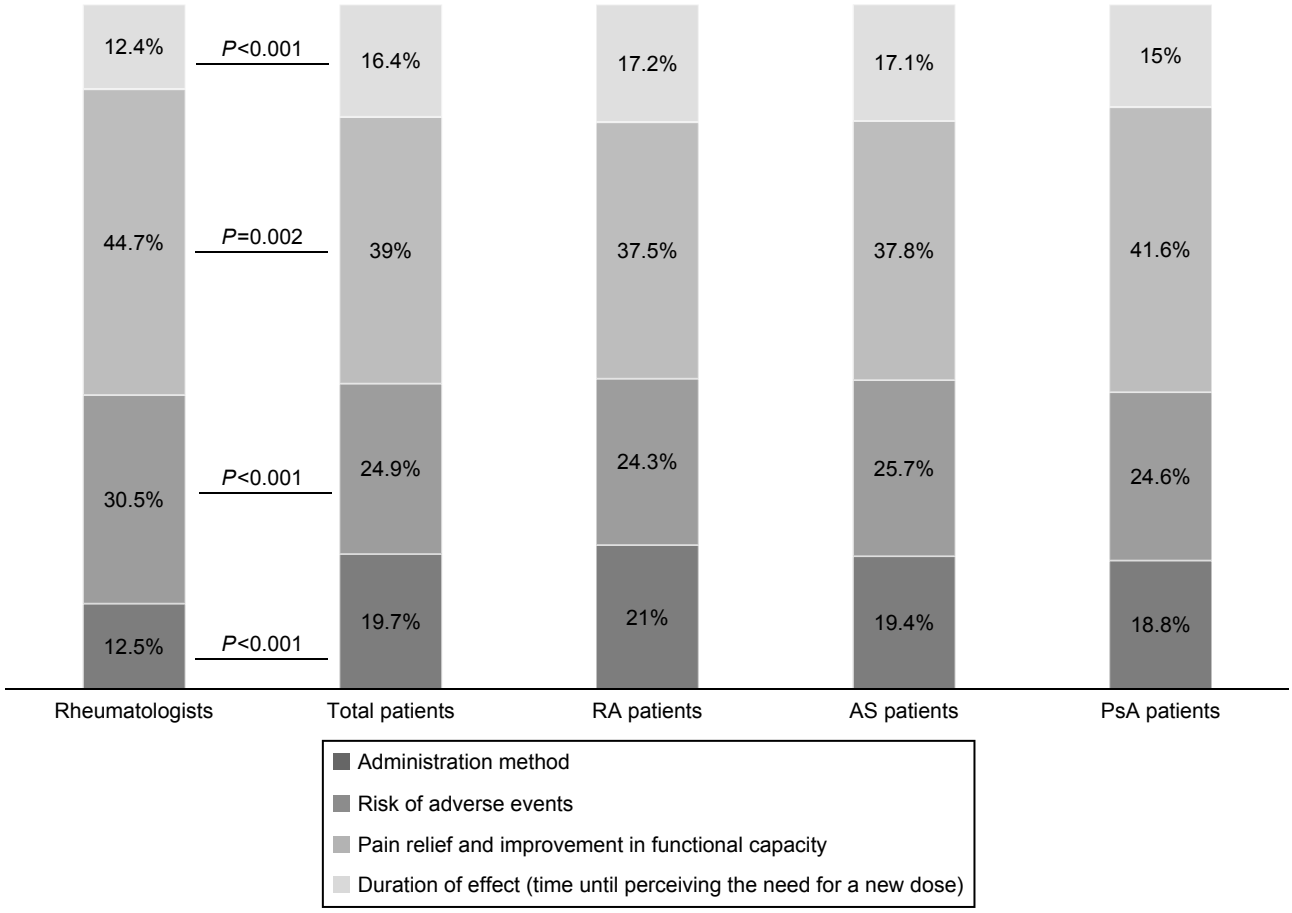

Figure 2 Relative importance values given by both patients and rheumatologists to the attributes of biological agents and for specific rheumatic conditions.
Abbreviations: RA, rheumatoid arthritis; AS, ankylosing spondylitis; PsA, psoriatic arthritis.

With regard to the time until perceiving the need for a new dose, both patients and professionals preferred 2–4 weeks over 1–2 weeks. Assuming that pain relief and risk of AEs were equal, patients' and professionals' utility values for BAs administered subcutaneously increased by 10% and 9% when the time until perceiving the need for a new dose was incremented from 4 to 8 weeks and by 20% and 17% when it was incremented from 1 to 8 weeks, respectively (Figure 3A and C). For BAs administered intravenously, the upturns for patients and professionals were 13% and 12%, and 25% and 23%, respectively (Figure 3B and D). These results demonstrate that both patients and rheumatologists gave higher importance to lower frequencies of administration or longer time until perceiving the need for a new dose.

The ideal BA for both patients and professionals would be a drug that relieved pain and improved ability to perform daily activities, with a low risk of side effects, self-administered at home subcutaneously, and with longer time until perceiving the need for a new dose (8 weeks).

Multivariate-regression analysis

Table 4 presents the results of the multivariate analysis, identifying the sociodemographic and clinical variables that affected the RI of each attribute. For patients, sex, pathology, symptoms, complications associated with the RD, and genitourinary comorbidities influenced the importance given to the risk of AEs. In general, females, patients diagnosed with AS, patients with articular rigidity, subjects without limitations to their functional capacity, and those with intestinal complications or genitourinary comorbidities gave greater importance to the risk of AEs. The variable that influenced the importance given to the relief of pain and improvement in functional capacity was disease symptoms. Patients presenting articular swelling and those without limitations in functional capacity gave less importance to the relief of pain. Mode of administration, age, sex, and the presence of intestinal complications influenced their preferences. Older patients, females, and those who presented an intestinal complication granted less importance to the mode of administration of BAs.

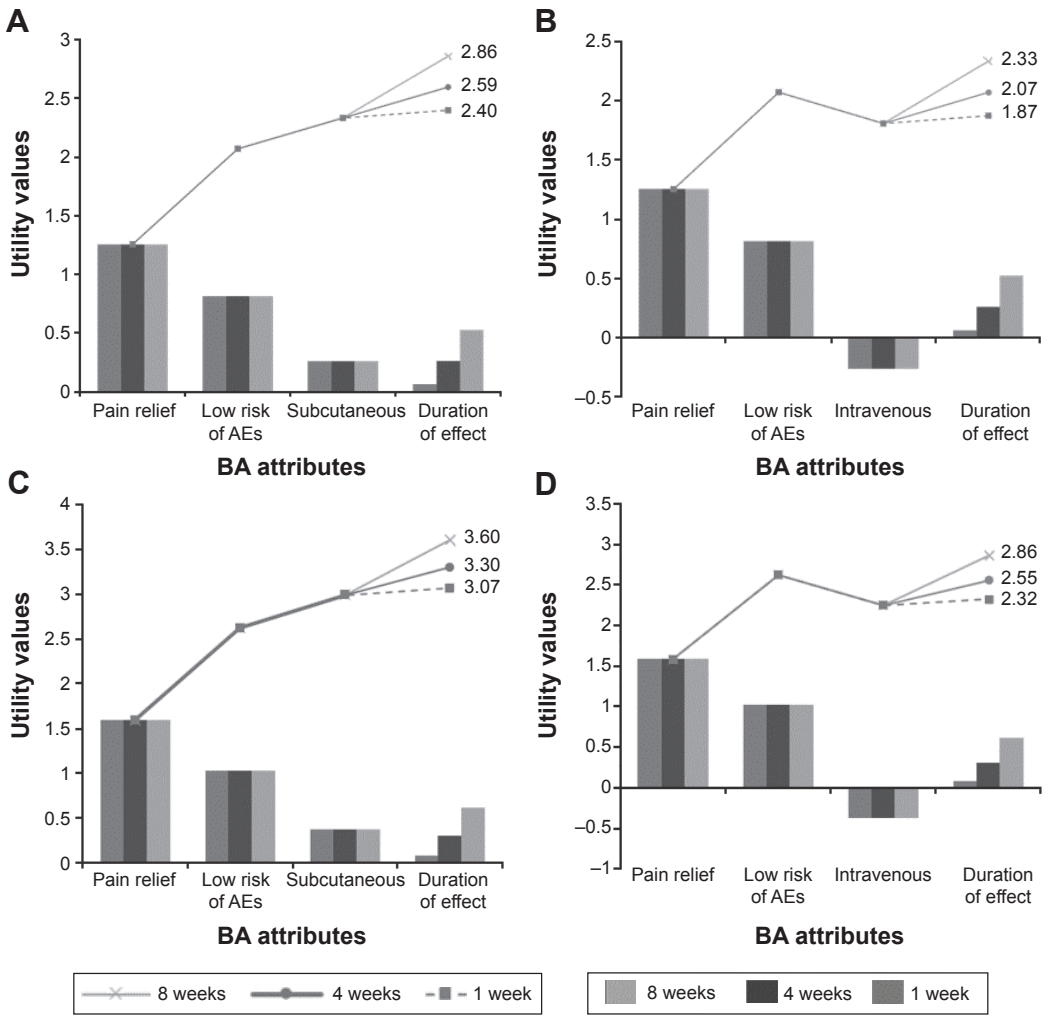

Figure 3 Pareto diagrams representing patients' and professionals' utility values for subcutaneous and intravenous treatment alternatives.
Notes: (**A**) Utility values for patients regarding subcutaneous treatment. (**B**) Utility values for patients regarding intravenous treatment. (**C**) Utility values for professionals regarding subcutaneous treatment. (**D**) Utility values for professionals regarding intravenous treatment. Duration of effect indicates the time until perceiving the need for a new dose (1 week, 4 weeks, and 8 weeks).
Abbreviations: AEs, adverse events; BA, biological agent.

For rheumatologists, age and length of their professional experience influenced the importance given to the risk of AEs. Older professionals and rheumatologists with less time practicing the specialty granted less importance to the risk of AEs. Sex influenced the importance given to the relief of pain and improvement in functional capacity. Females gave less importance to the relief of pain and improvement in functional capacity.

Discussion

In recent years, BA options for patients with RDs have continued to expand, creating opportunities for improved outcomes, such as decreased pain, disability, and mortality. However, patients as well as physicians are faced with increasingly complex decisions about how and when a medication should be prescribed.[32] It has been reported that health care professionals more often rely on personal beliefs and experiences to make clinical decisions than on scientific evidence,[33–35] and that those can differ from the views of their patients.[36] There is a need to provide patients with individualized treatment strategies and to enable their participation in medical decision making.[37] One essential factor that professionals must consider for reaching this goal is inquiring about patients' preferences.[38]

Results demonstrated that patients' and professionals' preferences were similar, the most to least preferred attributes being pain relief and improvement of functional capacity, risk of AEs, administration mode, and frequency of administration (time until perceiving the need for a new dose). The ideal treatment for both patients and professionals would be a BA that relieved pain and improved the ability to perform daily activities, with a low risk of AEs, self-administered at home subcutaneously, and with a greater time before perceiving the need for a new dose. Although efficacy and safety are

Table 4 Factors influencing patients' and rheumatologists' preferences[a]

Factors	Estimated coefficient	*P*-value
Patients		
Administration method		
Age	−5.72	0.0012
Sex (female vs male)	−10.45	0.0142
Intestinal complications (yes vs no)[b]	−11.05	0.024
Smoking habits: nonsmoker <1 year (vs smoker)	−0.61	0.8162
Smoking habits: nonsmoker >1 year (vs smoker)	1.12	0.6246
Smoking habits: never-smoker (vs smoker)	0.16	0.1019
Joint swelling (yes vs no)	4.27	0.0939
Joint rigidity (yes vs no)	−3.21	0.1185
Complications associated with RD (yes vs no)[b]	2.01	0.1111
Cardiac complications (yes vs no)[b]	−3.65	0.0619
Renal complications (yes vs no)[b]	−18.66	0.0227
Pulmonary complications (yes vs no)[b]	−11.21	0.0064
Neurological complications (yes vs no)[b]	9.4	0.0443
Genitourinary comorbidities not associated with RD (yes vs no)[b]	0.12	0.1221
Skin comorbidities not associated with RD (yes vs no)[b]	−2.86	0.1418
Risk of side effects		
Sex (female vs male)	5.08	0.0013
Pathology (AS vs RA)	4.12	0.0367
Joint rigidity (yes vs no)	4.48	0.0057
Limitation of functional capacity (yes vs no)	−5.42	0.0008
Intestinal complications (yes vs no)[b]	10.45	0.0083
Ocular complications (yes vs no)[b]	−5.55	0.0255
Genitourinary comorbidities (yes vs no)[b]	7.74	0.0237
BMI	−0.28	0.0666
Pathology (PsA vs RA)	1.58	0.3854
Pulmonary complications (yes vs no)[b]	8.42	0.0738
Osteomyoarticular comorbidities (yes vs no)[b]	−4.38	0.1352
Relief of pain		
Joint swelling (yes vs no)	−2.96	0.0283
Limitation of functional capacity (yes vs no)	6.76	0.0011
Age	−1.49	0.5293
Pathology (AS vs no AS)	4.28	0.0616
Pathology (PsA vs no PsA)	−6.72	0.0134
Renal complications (yes vs no)[b]	12.33	0.1574
Blood complications (yes vs no)[b]	10.15	0.1423
Skin complications (yes vs no)[b]	11.94	0.0852
Duration of effect		
Sex (female)	2.37	0.0836
BMI	0.22	0.1273
Regular alcohol consumption (no vs yes)	−3.17	0.084
Symptom duration	−0.13	0.0581
Endocrine comorbidities (yes vs no)[b]	−2.3	0.1521
Circulatory comorbidities (yes vs no)[b]	3.63	0.0828
Congenital anomalies/comorbidities (yes vs no)[b]	−22.11	0.1096
Rheumatologists		
Administration method	NA	NA
Risk of side effects		
Age	−1.31	0.0007
Duration of professional exercise	1.03	0.0099
Relief of pain		
Sex (female vs male)	−6.39	0.0329
Age	0.3	0.0662
Time until perceiving the need for a new dose		
Age	0.59	0.0396
Sex (female vs male)	3.88	0.0256
Duration of professional practice	−0.61	0.04

Notes: [a]Results from multivariate regression analysis; [b]according to physician's judgment. The coefficients of the quantitative variables indicate the magnitude of change in the independent variable for each unit of increase in the dependent variable. In the qualitative variables, coefficients indicate the change in the variable response with respect to the reference category (positive values indicate increase; negative values indicate decrease).

Abbreviations: BMI, body mass index; RA, rheumatoid arthritis; AS, ankylosing spondylitis; PsA, psoriatic arthritis; RD, rheumatic disease; NA, not applicable.

key aspects for participants, both the frequency and method of administration play an important role as attributes of BAs in Spain. In this study, both patients and professionals preferred a low frequency of administration. Huynh et al[32] recently presented similar results. In an observational study performed in Denmark including RA patients naïve to and treated with BAs, as well as physicians and nurses, low treatment frequency was the preferred attribute for patients, followed by a more conservative route of administration. The authors concluded that the route and frequency of administration could influence patients' adherence to and satisfaction with the treatment. Parallel outcomes were reported by Augustovski et al,[39] who performed a discrete-choice experiment on patients with RA naïve to BAs. These authors showed that avoidance of systemic AEs was the preferred attribute of BAs, followed by frequency of administration, efficacy, and route of administration.

In the present work, the RI given to the mode of administration and to the time until the perception of the need for a new dose was significantly greater in patients, while professionals placed more importance on the relief of pain, improvement in functional capacity, and risk of AEs. These differences could be due to patients granting more value to the characteristics regarding treatment comfort or convenience, while these aspects are not so valued by rheumatologists. These results are also in line with the previous findings of Huynh et al,[32] where RA patients and health professionals showed similar preferences regarding the route and frequency of administration of BAs, especially with those patients receiving subcutaneous treatment, but with differences in magnitude.

The importance of the administration route was also demonstrated in a study performed in Italy,[40] in which patients with RA addressed their perceptions of their current treatment and preferences for anti-TNF agents. The findings showed that 50.2% of patients preferred intravenous administration, mainly due to the reassuring effect of the presence of health care personnel, while 49.8% chose subcutaneous administration for its convenience. Moreover, in a study conducted in the UK[41] to assess the preferences of patients with RA receiving anti-TNF therapy or conventional DMARDs, the route of administration was the single feature of anti-TNF therapy that concerned patients the most. Subcutaneous injection was the first choice for those on anti-TNF therapy (41%) and those not yet receiving BAs (52.5%).

This analysis has some limitations, due to its design. The number and definition of attributes and factor levels is the critical step in any conjoint analysis, and although it followed the available guidelines, as it was based on a literature review and the opinion of patients and professionals, it may be subject to biases, due to participants' cultural context or experience. Further research is needed to determine the relative effect of other potentially important attributes not included in this study, and to evaluate the stability of results across different populations. Moreover, patient preferences need to be explored in more depth in populations at a higher risk of poor communication with their physicians (those with low literacy, lower levels of education, and immigrants) and at risk of incomplete understanding or misunderstanding of the risks and benefits of these medications. Considering that this study was restricted to patients and rheumatologists from the Spanish public health system, its results must be extrapolated carefully to subjects from different backgrounds and cultures, patients with more severe diseases or institutionalized, or rheumatologists with less clinical experience than the included population, and must be interpreted within the context they were performed. Furthermore, a period of at least 1 year in biological DMARD (bDMARD) experience was chosen to select patients for this study, so it has to be considered that patients with early discontinuation of bDMARDs could have expressed different preferences.

For missing data, there are no objective criteria to clarify the maximum percentage of omissions that can be accepted, so each researcher must be responsible for their own decisions.[42] In the case of this study, given that all data were available for main variables (conjoint analysis), and that the maximum percentage of missing data for secondary variables was just 2.5%, missing values were not imputed, and results were calculated from available data. Nonetheless, this study provides very interesting results.

To the authors' knowledge, it is the first time the preferences of treatment-experienced Spanish patients with different RDs, and rheumatologists, have been examined and their needs and perceptions regarding BAs identified and compared by means of a ranking-based conjoint analysis. Understanding patient needs provides the physician with the basis for the right therapeutic choice.[43,44] At the same time, physician preference has been shown to be an important determinant of patient acceptance of biological therapy,[45] so the physician perspectives were also assessed in this study and compared to those of patients. This approach allowed us to detect differences between these two perspectives.

The knowledge produced in this analysis could contribute to a more informed decision-making process and a better choice of treatments.[46] Professionals should thus explore the preferences of patients by involving them in treatment decisions,[28] in order to achieve improvement in the quality of their care.[47]

Conclusion

The assessment of patients' and professionals' preferences for the different attributes of BAs in the treatment of RDs is a necessary step toward improving results, by ensuring satisfaction and adherence findings that could contribute to better outcomes. Spanish patients with RDs' and rheumatologists' preferences for BAs were similar, preferring medication that relieves pain and improves ability to perform daily activities, with a low risk of AEs, self-administered at home subcutaneously, and with a greater time before perceiving the need for a new dose. Although efficacy and safety are key aspects for participants, both the frequency and method of administration play an important role as attributes of BAs.

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Disclosure

JM Nolla, M Rodríguez, E Martin-Mola, E Raya, and I Ibero report they have received remuneration for their contribution

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