PATIENT PREFERENCES IN THE CHOICE OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with a variety of systemic manifestations, the characteristic feature being persistent inflammatory synovitis of peripheral joints in symmetric distribution causing cartilage damage and bone erosion[1]. The prevalence across Europe varies by population between 0.32% (France) to 0.83% (UK)[2]. There is a variety of biologic and conventional synthetic disease modifying anti-rheumatic drugs (DMARDs) available for the treatment of RA. DMARDs are associated with different characteristics in key attributes such as route of administration, frequency of administration etc. Importantly, biological DMARDs (bDMARDs) are all administered parenterally[3]. However, targeted synthetic DMARDs offer alternative administration forms (i.e. oral administration). To address patient preferences and to inform decision making regarding this aspect, a quantitative approach is needed. The current study assesses the importance of such treatment characteristics for RA patients' preferences using a discrete choice experiment (DCE) in an ecologically valid design.

Methods

Study Design

In a questionnaire-based DCE, 1570 RA patients are asked to choose the most and least preferred DMARD (best-worst-scaling) among hypothetical multi-attribute treatment options with varying levels of key attributes, as defined in focus groups. Choices are repeated in a "d-efficient" design[4] with multi-attribute treatments, i.e. decision scenarios involving different products with varying levels of the same attributes (see **Figure 1**). D-efficient designs allow assessing attributes' levels' main effects on participants' choices, i.e. part-worths (utilities), by minimizing correlations between different levels across scenarios under given constraints. A design with multi-attribute products (multi-profile case) simulates a real choice situation between different treatment alternatives. Each questionnaire includes eight DCE scenarios. Interim analysis was conducted on half the sample size.

Assessments

In addition to the DCE, patient-related variables are assessed: age; gender; disease duration; DMARD medication; disease severity (RADAI-5[5]); beliefs about efficacy/tolerability, necessity/concern[6] regarding current DMARD medication (using a modified BMQ[7]); comorbidity (SCQ-D[8]).

Fig. 1: Example of a DCE scenario as used in the questionnaire

	Treatment 1	Treatment 2	Treatment 3
mode of administration	*subcutaneous self-injection*	*intravenous infusion*	*pill*
frequency of administration	*once every 6-12 months*	*once every 1-2 weeks*	*twice daily*
time till onset of drug effect	*up to 1 month*	*more than 1 till up to 3 months*	*up to 1 month*
combination therapy	*yes: MTX once a week*	*no, not necessary*	*yes: MTX once a week*
safety issues	*allergic reactions*	*deterioration of laboratory values*	*Infections*
treatment I like best	X		
treatment I find worst		X	

Note: As a constraint, unrealistic level combinations ("infusion, two times daily" and "oral intake, once every 6 to 12 months") were excluded from the design.

Results

Study Population

For interim analysis, questionnaires from 836 patients had been received. To this stage, patient had been recruited from 33 office based rheumatologists across Germany. The majority of patients are female (74%, N = 619), 50 to 64 years of age (46%, N = 471) with <10 years of disease duration (54%, N = 448) – reflecting typical epidemiological characteristics of the RA patient population[2]. Most patients (63%) report mild to moderate disease activity according to RADAI-5 (**Figure 2**). Common co-morbidities include: back pain (47%, N = 396), arthritis (42%, N = 348), hypertension (40%, N = 336), and gastrointestinal problems (19%, N = 159).

Fig. 2: Disease activity

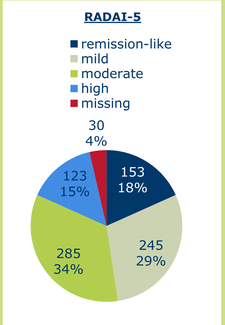
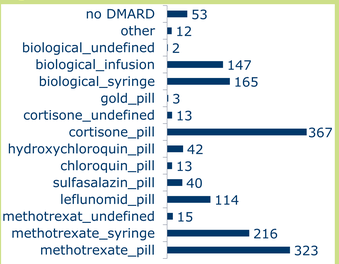


Fig. 3: Current DMARD status



Note: If route of administration cannot be determined, medication is labeled "undefined".

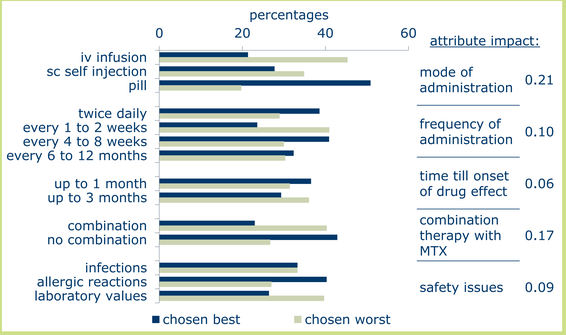
Figure 3 depicts counts for reports of current DMARD medication: The majority of patients is currently receiving methotrexate (MTX) (N = 543, 65%) of whom 34% (N = 186) are using it as mono-therapy and 45% (N = 244) in combination with cortisone. About a third is receiving bDMARDs (N = 310; 37%) of whom 27% (N =83) are using them as mono-therapy, 48% (N = 149) in combination with methotrexate, and 47% (N = 144) in combination with cortisone. 63% of the patients (N = 530) report prior experience with injectable DMARDs from current or previous treatments. The majority (~85%) reports being satisfied with their current treatment's overall efficacy (N = 709) and tolerability (N = 707), and is "accepting" towards their current DMARD medication (63%, N = 523; i.e., patients believe taking their medication is of high necessity and low concern[6]). A still remarkable proportion (19%, N = 162) reports an "ambivalent" attitude towards their DMARD medication (i.e., taking medication is of high necessity but also high concern[6]).

DCE Analysis

Count analysis[9]: Part-worths (utilities) are based on percentages of how often a level is picked as best and worst across its total times of presentation. The difference between best and worst choice percentages reflects a level's influence on choices, with larger differences indicating stronger influences (results see **Figure 4**).

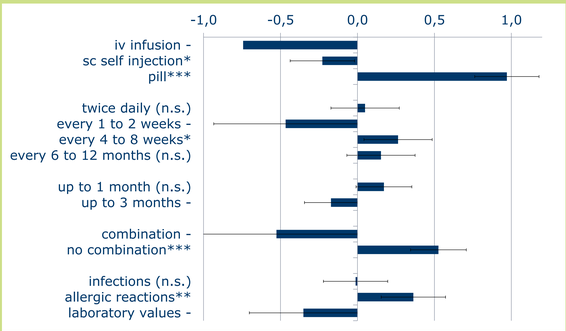
Regression analysis[10]: Predicts counts of levels simultaneously chosen as best and worst across DCE scenarios to estimate the levels' influences on patients' choices; β-weights from regression equation are interpreted as levels' part-worths. Unlike count analysis, regression analysis allows inferring statistical significance of the levels' influences (results see **Figure 5**).

Fig. 4: Results of count analysis



Note: Attribute impact is the average of the attribute's levels' best and worst choice percentage differences, i.e. (Σ|(% chosen best – % chosen worst)|/number of levels).

Fig. 5: Results of regression analysis



Note: Negative β-weights indicate a level predominantly picked as worst, thus considered unfavorable (negative utility); positive β-weights indicate a level predominantly picked as best, thus considered favorable (positive utility); * p<.05, **p<.01, ***p<.001, n.s.=not significant, -=reference level in effect coding.

Conclusions

The present study aims to determine the relative importance of DMARD characteristics for RA patient preferences. Analyses are based on an RA sample with typical epidemiological characteristics – suggesting a representative sample – and prior experience with injectable DMARDs by majority. Among attributes included in the study, route of administration appeared most important in guiding patients' preferences, with oral application being most desirable (selected as best in 51% and worst in only 20% of cases). Necessity to combine one's treatment with methotrexate yielded second most important attribute, with no need for combination therapy being preferred (in 43% of cases). **Therefore, an oral DMARD that does not have to be combined with methotrexate appears a highly favorable second-line treatment option for RA patients.**

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