A Nationwide Survey on Patient's versus Physician´s Evaluation of Biological Therapy in Rheumatoid Arthritis in Relation to Disease Activity and Route of Administration: The Be-Raise Study

Sophie De Mits[1]ʘ, Jan Lenaerts[2]ʘ, Bert Vander Cruyssen[3], Herman Mielants[1], René Westhovens[4], Patrick Durez[5], Dirk Elewaut[1,6]*, on behalf of the Be-Raise study group[¶]

1 Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, 2 Department of Rheumatology, Reuma-Instituut Hasselt, Leuven University Hospital, Leuven, Belgium, 3 Department of Rheumatology, Sint Jozef Hospital Bornem, OLV Hospital Aalst, Aalst, Belgium, 4 Skeletal Biology and Engineering Research Center, Department of Development and Regeneration KU Leuven; Rheumatology, University Hospitals Leuven, Leuven, Belgium, 5 Department of Rheumatology, Université Catholique de Louvain UCL, Louvain-la-Neuve, Belgium, 6 Laboratory of Molecular Immunology and Inflammation, VIB Inflammation Research Center, Ghent University, Ghent, Belgium

ʘ These authors contributed equally to this work.
¶ Membership of Be-Raise study group is provided in the Acknowledgments.
* Dirk.Elewaut@UGent.be

Abstract

Objectives

Biological treatment of rheumatoid arthritis (RA) is one of the cornerstones of current treatment strategies for the disease. Surprisingly little information exists on whether the route of administration affects patients' treatment satisfaction. It is equally unclear whether rheumatologists are able to accurately perceive their patients' appreciation. Thus, the Belgian Be-raise survey aimed to examine whether RA patient's experience of their current biological treatment coincided with the treating physician's perception.

Methods

A nationwide cross-sectional survey was conducted by 67 Belgian rheumatologists providing data obtained from 550 RA patients. Patients under stable dose of biologics for at least 6 months, were enrolled consecutively and all completed questionnaires. Separate questionnaires were completed by the treating rheumatologist which evaluated their patient's perception of the route of treatment administration. This study therefore evaluates whether a treating physician perceives the satisfaction with the route of administration to the same degree as the patient.

Results

Completed questionnaires were obtained from 293 and 257 patients who obtained treatment via the intravenous (IV) or subcutaneous (SC) route of administration, respectively.

58.4% of patients were in DAS28-CRP(3) remission. Patient satisfaction with disease control was higher (44% scored $\geq$ 9) than that of the treating physician (35%), regardless of the route of administration (p< 0.01). No differences were seen for the patients treated with an IV as opposed to a SC route of administration. The physician´s perception of patient's satisfaction with disease control was markedly lower for IV treated patients as opposed to SC treated patients (p< 0.001).

Conclusions

Patients' satisfaction with biological treatment is high, but there is a considerable mismatch between patients´ and rheumatologists´ appreciation on the route of administration of biological therapy in RA. Physicians consistently consider IV biological therapy to be less satisfactory. Patient´s appreciation is largely dependent on disease control, irrespective of the route of administration. Therefore, and encouraging shared decision making, we suggest that physicians and patients discuss the route of administration of biologicals in an open way.

Introduction

Over the past two decades the introduction of biologics has caused a paradigm shift in the treatment of diseases such as rheumatoid arthritis (RA). The efficacy of these biologicals has been evaluated in clinical trials using classical clinical outcome measures such as ACR20, HAQ, X-ray scores and DAS28 [1, 2]. Incorporating outcome measures such as DAS scores, imaging, as well as an evaluation of the patient's quality of life has changed treatment targets in clinical practice and improved patient outcome.

In recent years the development of pre-filled syringes has promoted subcutaneous (SC) administration of biologicals and has therefore become an attractive alternative to an intravenous (IV) route of administration [3]. In this context, several studies have investigated the efficacy and safety of different biological therapies available in either IV or SC formula (eg. abatacept, golimumab, adalimumab, tocilizumab) and found no difference between these modes of administration [2, 4–6].

Although the route and frequency of administration might affect the adherence to treatment [7, 8], to date only a limited number of studies have examined the patients' preference for one route of administration above another [7–12]. The majority of patients appear to prefer a SC route of administration for biologicals [8–10, 12], with only one study showing no preference between either IV or SC administration [7]. In this context, factors favoring IV infusion of biologicals in patients include: the safety of hospital administration and the presence of medical staff, social contact in the hospital, patient compliance and the possibility for regular checkups. Factors supporting a SC route on the other hand include: the comfort and convenience of treatment at home, avoiding/minimizing time of transportation for treatment, improving the quality of life due to less interference with the everyday life and the feeling of greater independence, freedom and the capacity for self-management [1, 5, 7, 8, 11, 13]. Age, frequency of administration, re-imbursement for one admission mode versus the other and confidence in the treating physician decision might also be of influence for the patient preferences for either the IV or SC route of administration [7, 8, 14–17].

Although the treatment choice should preferably be a shared patient–physician decision, as stated in the Eular recommendations [18], the physician's judgment and the patient's trust in

the physician seem to have a greater effect on the confidence in the treatment decision rather than the patient's knowledge of potential treatment options [16, 18, 19]. However, involvement in the decision-making process might enhance patient's satisfaction with and adherence to therapy [10].

Since the physician's opinion plays an important role in the patient choice of route of administration, it seems important to know if the patient and the physician would make the same choice if they make this independently from one another. Thus far, to our knowledge, only two studies have questioned health professionals about their preference for one route of administration above another (ie. IV vs SC). In one study physicians were asked to complete a questionnaire as if they were patients themselves [7]. In contrast, Willeke et al. conducted a survey of RA patients' and of rheumatologists' preferences for IV or SC administration. However, the rheumatologists were not the treating physicians of the patients participating in the study [20].

Thus, we propose that both patient and treating physician alike may benefit from a study which investigates how each party experiences the treatment of RA. Factors that are of interest here include the general satisfaction of disease control as well as the convenience of the route of administration of current biologics.

We therefore initiated a nationwide survey called Be-Raise (Belgian Rheumatoid Arthritis: Patient Insights, Strategies and Expectations), which aimed to investigate how patients and their treating physicians experience treatment of RA. In addition, this study investigated if patient's and physician's perception was similar.

Materials and Methods

Be-Raise is a nationwide cross-sectional survey, which invited all Belgian rheumatologists to participate. RA patients under a stable biological therapy for at least 6 months were selected consecutively in an outpatient clinic or day-hospital. This selection was made to avoid patients that were still in a phase of therapy adjustment with a biologic. In all participating practices, each rheumatologist could include a maximum of 10 RA patients. The study was approved by the Ethical Committee of Ghent University Hospital.

Both patients and physicians completed a similar questionnaire, newly constructed for this purpose. The difference in the questionnaires can be seen in the phrasing: the patient's version uses the words 'you' and 'yours', whereas the physician's version uses the words 'your patient'. Furthermore, the patient's version started with collecting data about age, sex, date of diagnosis, employment and marital status. The physicians were asked about their years of experience as a rheumatologist and about their clinical setting (academic/peripheral/private practice, rheuma nurse availability). The physicians also provided some extra patient information about the current disease activity (CRP, ESR, global VAS, joint score).

Since SC treated patients have a different participation in their therapy compared to IV treated patients, the phrasing of the questionnaires was adapted to the route of administration. The patient's questionnaires pertaining to SC or IV administration differed only in the questions concerning administration. More specifically, patients receiving biologics intravenously were asked to score the treatment within a hospital setting whereas patients administered biologics subcutaneously were asked to score for more variables. The SC patient had to choose between the section 'you are self-administering your biological treatment' or 'your biological treatment is given at home by someone else than yourself' and received additional questions pertaining to drug preparation and storage. Table 1 summarizes what was asked of patients and physicians in the questionnaires. The full version of the questionnaires can be found in the supplementary material (S1–S3 Questionnaires).

Table 1. The different items covered by the questionnaires.

The patient's questionnaire
• demographic data
• medication use: biological and concurrent medication for rheumatoid arthritis
• how the choice for biological treatment was made
• the evaluation and satisfaction of the effect of their biological treatment on symptoms and daily live activities
• the practical aspects of their treatment and the satisfaction with the way of administration
• therapy compliance
• the knowledge about and attitude towards possible side effects during treatment with biologicals
• the preference of administration (regardless of their current form of therapy)
The physician's questionnaire
• information about the physician's experience and clinical setting
• information about the patient: disease duration and disease activity, medication
• how the choice for the biological treatment was made
• the evaluation and satisfaction of the effect of the patient's biological treatment on symptoms and daily live activities
• the practical aspects of the patient's treatment and his/her satisfaction with the way of administration
• the patient's therapy compliance
• the patient's perception about the safety of the use of biologicals

doi:10.1371/journal.pone.0166607.t001

Patients and treating physicians completed questionnaires independently of one another and in a blinded fashion. At the central collection point, the coded questionnaires were merged and a supplemental control of matching was performed by verifying sex and age.

Most questions about satisfaction were reported on a 0–10 Likert scale. Good satisfaction was defined by a score of ≥ 9.

Statistics

Descriptive analyses were included in the calculations of proportions for categorical variables and means/medians with 95% confidence intervals.

DAS28 was calculated according to the DAS28-CRP(3) formula. DAS28-CRP(3) was used as the standard covariate in regression analyses, but all regression analyses were double checked with the DAS28-ESR(3). Generalized linear model analysis was used with a logit link for dichotomous data and an identity link for continuous data. Missing data were handled by the 'missingness completely at random' (MCAR) assumption [21]. Propensity scores were calculated as described by Joffe & Rosenbaum [22].

All statistics were calculated with PASW 18 "SPSS 18" (Chicago, Illinois, US).

Results

Of the 200 registered Belgian rheumatologists, 67 (30%) of those working in 37 private practices and outpatient settings of hospitals participated in this study. Questionnaires were obtained from 550 patients of which 293 received drugs IV and 257 SC. Physician-patient matched questionnaires were obtained for 260 IV and 231 SC treated patients, respectively. Missing value analyses did not suggest against the MCAR assumption. While we have not recorded the information of non-included patients in all centers, data from one center (Ghent University Hospital) would not suggest that this is the case as included patients did not differ in all characteristics (such as DAS28) compared to non-included patients.

Table 2. Demographic and baseline characteristics.

	all	IV	SC
age (years)	57.7 ± 12.34	57.7 ± 12.16	57.8 ± 12.56
gender			
male (n)	114 (20.7%)	63 (23.2%)	51 (21.3%)
female (n)	389 (70.7%)	205 (75.4%)	184 (76.7%)
missing (n)	47 (8.5%)		
disease duration (years)	3.3 ± 0.81	3.4 ± 0.80	3.3 ± 0.83
clinic type			
university hospital (n)	199 (36.2%)	129 (47.54%)	65 (27.1%)
private hospital (n)	188 (34.2%)	92 (33.8%)	74 (30.8%)
private outpatient clinic (n)	133 (24.2%)	34 (12.5%)	88 (36.7%)
missing (n)	30 (5.2%)	17 (6.2%)	13 (5.5%)
CRP (mg/l)	12.4 ± 55.83	14.1 ± 74.7	10.3 ± 29.02
ESR (mm/h)	15.0 ±18.51	16.4 ± 16.7	13.2 ± 19.93
global VAS (mm)	23.7 ±20.77	21.6 ± 19.3	25.5 ± 22.02
DAS-28-3 CRP	2.6 ±1.06	2.5 ± 1.02	2.6 ± 1.11
remission (n)	321 (58.4%)	167 (61.4%)	138 (57.5%)

IV: intravenous, SC: subcutaneous, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate

doi:10.1371/journal.pone.0166607.t002

The demographic and baseline characteristics of patients and the treatment they received are shown in Table 2. There were no differences between the IV group and the SC group. Patients (n = 550) were treated with Etanercept (17.1%), Adalimumab (25.6%), Certolizumab (0.9%) Golimumab (2.7%), Rituximab (10.0%), Abatacept (8.7%), Infliximab (20.9%) or Tocilizumab (14%).

Further analysis was performed only on matched (physician–patient) questionnaires.

Patient's and physician's satisfaction with control of RA symptoms

The patient's satisfaction on the overall control of RA symptoms was higher than the treating physician's, regardless of the route of administration. 44% of patients were satisfied (score $\geq$ 9) about symptom control, compared to 35% of the treating physicians (OR = 3.9 (2.6–5.8) p < 0.001) (Fig 1 panel A). Furthermore, no differences were seen for the patients treated with an IV compared to a SC route of administration.

Patient's and physician's satisfaction with the route of therapy administration (IV vs SC)

Conversely, the physician´s perception of patient's satisfaction with disease control was noticeably lower for IV treated patients as opposed to SC treated patients. Here, 70% of physicians estimated that IV treated patients were less satisfied with an IV route of administration (Fig 1 panel B) as opposed to 54% for SC treated patients (OR = 1.9 (1.4–2.8) p< 0.001).

Further logistic regression analyses, corrected for a propensity score for IV/SC allocation (including sex, age, professional status and disease duration etc.) revealed that patients are significantly more satisfied with the route of administration when they are also comfortable about disease control (OR = 4.1, 95% CI 2.7–6.2 p<0.0001). In contrast, neither the route of administration (OR = 0.77, 95% CI 0.46–1.27, p = NS) nor the frequency of administration (OR = 0.71,95%CI 0.47–1.07, p = NS) affected the appreciation of therapy administration.
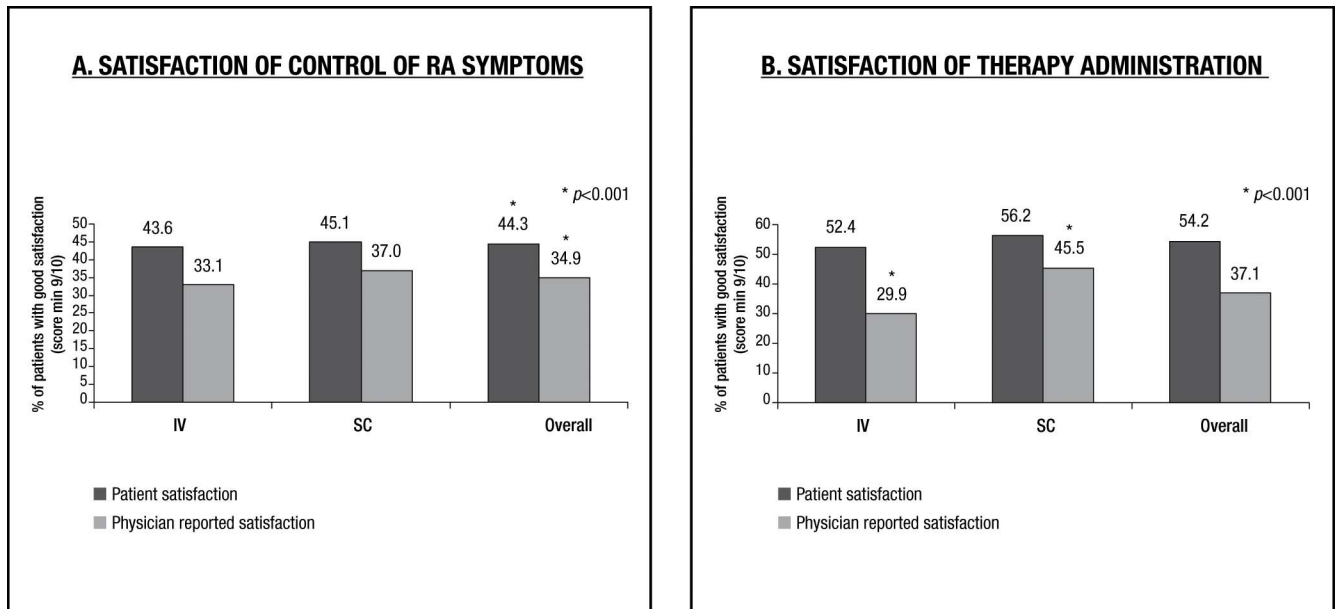
Fig 1. Patient satisfaction and associated physician's opinion of control of RA symptoms and on therapy administration. IV: Intravenous; SC: subcutaneous.

Finally, the physician's preferred therapy administration differs from that of the patient's. IV use was consistently rated lower than SC use (OR = 0.531, 95% CI = 0.302–0.934, p = 0.028), irrespective of disease activity or frequency of therapy administration. Different sensitivity analyses with continuous data (generalized linear modeling with identity link) and alternative DAS formulas confirmed these findings.

Discussion

The results from this nationwide study highlight that in approximately 50% of the cases recorded, patients´ and rheumatologists´ judgement differ in the context of disease control and the degree of satisfaction related to the route of administration of biological therapy in RA. Physicians consistently consider IV biological therapy to be less satisfactory, whereas the patient´s appreciation is independent of the route of administration. This study underlines the finding that the primary factor promoting patient satisfaction is good disease control.

The finding that 52.4% of patients were satisfied with an IV route of administration as opposed to 56.2% of patients receiving SC administration is in accordance with previous studies which show a preference for SC over IV administration of biologicals [8–10, 12].

Although age has been shown to influence a preference for IV above SC drug administration in patients [7, 8, 17], within our patient population there was no significant difference (p = 0.70) between the mean age for the IV or SC group, being 57.7 ± 12.16 years and 57.8 ± 12.56 years, respectively.

Distance and time to treatment and re-imbursement have been named as possible factors influencing the choice of treatment [7, 8, 11, 17]. Within Belgium's social and economic context, this might be of minor importance. It is a small country with good accessibility to different hospitals and out-patient clinics and the patient is free to choose his specialist. Biological therapy can only be prescribed by a rheumatologist, guided by restricted rules concerning reimbursement. However, these rules are the same for the different biological therapies and

for the different routes of administration, and are therefore of no influence in the decision on IV or SC administration [7–10, 12, 17].

Although our questionnaire did not explicitly address whether physicians preferred one route of drug administration above another, we assume they rank oral administration above SC and IV administration, respectively. However, for a patient with a chronic potentially disabling disease, it would appear that the route of administration is of less importance to the patient as long as the treatment is effective. Thus, encouraging shared decision making, we suggest the physicians to discuss this matter in an open way.

The findings of this study are in agreement with results presented by Willeke et al. where it is suggested that rheumatologists overestimate the preference of patients for SC injections. Willeke et al. revealed 88% of physicians preferring the SC mode and 92% of the physicians assumed that patients would do so as well, while 92% of the patients would choose again for intermittent IV therapy [20]. In this study it was shown that 52,4% of patients were satisfied with an IV route of administration whereas only 29.9% of their treating physicians thought they were pleased with the IV route of administration.

To our knowledge, this study is the first to compare patients' and physicians' evaluation on the route of administration. This large nationwide dataset, allowing adjustments with regression analysis, and the blinded comparison of patients' and physicians' opinion on a large set of questions, reinforces the findings of this study. Nevertheless, this study is limited by the cross sectional design and these results have to be interpreted within Belgium's social and economic context.

Currently, patient participation in treatment decision making is actively encouraged. It is also known that a patient's trust in his/her physician has a significant effect on the confidence in the type of treatment prescribed. Thus, future studies should address the degree of discrepancy between the rheumatologist's and patient's perception, preference and expectations for a specific treatment regime. Furthermore, how the frequency of drug administration affects the choice of treatment also requires further study.

Conclusion

In conclusion, this study demonstrates patient's preference and satisfaction for a biological treatment to be independent of the route of administration, but primarily to be driven by the patient's satisfaction about the treatment effectiveness. In contrast, physicians consistently consider IV biological therapy to be less satisfactory for patients.

Supporting Information

S1 Questionnaire. Be-Raise Questionnaire patient_IV.
(PDF)

S2 Questionnaire. Be-Raise Questionnaire patient_SC.
(PDF)

S3 Questionnaire. Be-Raise Questionnaire physician.
(PDF)

Acknowledgments

Contributors

Members of the Be-Raise study group are: Prof.MIELANTS Herman, UNIVERSITAIR ZIE-KENHUIS GENT De Pintelaan 9000 GENT; Dr.STUER Ann, HEILIG HART ZIEKENHUIS Wilgenstraat 8800 ROESELARE; Dr.VAN DE VYVVERE Klaas, AZ GROENINGE Burgemee-ster Vercruysselaan 8500 KORTRIJK; Dr.GYSELBRECHT Lieve, ALGEMEEN STEDELIJK ZIEKENHUIS Merestraat 9300 AALST; Dr.VAN DEN BERGHE Marthe, ALGEMEEN STE-DELIJK ZIEKENHUIS Merestraat 9300 AALST; Dr.ACKERMAN Christine, ST. LUCASZIE-KENHUIS Groene Briel 9000 GENT; Dr.JANSSENS Xavier, ST. LUCASZIEKENHUIS Groene Briel 9000 GENT; Dr.STAPPAERTS Geert, PRIVATE PRACTICE Molenstraat 9820 MERELBEKE—SCHELDERODE; Dr.DHONDT Eric, AZ ST JAN Ruddershove 8000 BRUGGE; Dr.MAERTENS Martin, AZ DAMIAAN Gouwelozestraat 8400 OOSTENDE; Dr. LENSEN Filip, AZ ST JAN CAMPUS SERRUYS OOSTENDE Kairostraat 8400 OOSTENDE; Dr.HERMAN Helena, AZ ST. BLASIUS Kroonveldlaan 9200 DENDERMONDE; Prof.DE CLERCK Luc, UZ ANTWERPEN Wilrijkstraat 2650 EDEGEM; Prof.VAN OFFEL Jan, UZ ANTWERPEN Wilrijkstraat 2650 EDEGEM; Dr.LECHKAR Bouchra, UZ ANTWERPEN Wilrijkstraat 2650 EDEGEM; Dr.DE CLERCQ Luc, SINT AUGUSTINUS ZIEKENHUIS Oos-terveldlaan 2610 WILRIJK; Dr.HOFFMAN Ilse, SINT AUGUSTINUS ZIEKENHUIS Ooster-veldlaan 2610 WILRIJK; Dr.LENAERTS Jan, REUMA INSTITUUT Anna Frankplein 3500 HASSELT; Dr.VAN WANGHE Paul, REUMA INSTITUUT Anna Frankplein 3500 HAS-SELT; Dr.LANGENAKEN Christine, REUMA INSTITUUT Anna Frankplein 3500 HASSELT; Dr.CORLUY Luk, REUMA INSTITUUT Anna Frankplein 3500 HASSELT; Dr.RAEMAN Frank, PRIVATE PRACTICE Bredabaan 2170 MERKSEM; Dr.JOOS Rik, PRIVATE PRAC-TICE Bredabaan 2170 MERKSEM; Dr.VERBRUGGEN Ann, PRIVATE PRACTICE Breda-baan 2170 MERKSEM; Dr.MAENAUT Kristin, PRIVATE PRACTICE Albert Dineurlaan 2900 SCHOTEN; Dr.REMANS Philip, REUMACENTRUM Weg naar As 3600 GENK; Dr. REMANS Jan, REUMACENTRUM Weg naar As 3600 GENK; Dr.VAN DEN BOSCH Filip, PRIVATE PRACTICE Hendrik Heymanplein 9100 ST NIKLAAS; Dr.WILLIAME Lucas, ZNA MIDDELHEIM Lindendreef 2020 ANTWERPEN; Dr.DECLERCK Kathleen, PRIVATE PRACTICE Schuttersvest 2800 MECHELEN; Dr.BRASSEUR Jean-Pierre, CLINIQUE ST, PIERRE Avenue Reine Fabiola 1340 OTTIGNIES; Dr.BRIGODE Michel, CLINIQUE ST, PIERRE Avenue Reine Fabiola 1340 OTTIGNIES; Dr.TOUSSAINT Francis, CLINIQUE ST, PIERRE Avenue Reine Fabiola 1340 OTTIGNIES; Dr. ANDRE Béatrice, CHU SART TIL-MAN Domaine Sart Tilman 4000 LIEGE; Dr.RIBBENS Clio, CHU SART TILMAN Domaine Sart Tilman 4000 LIEGE; Dr.JEUGMANS Anne-Marie, CHU LIEGE SITE NOTRE DAME DES BRUYÈRES Rue de Gaillarmont 4032 CHENEE; Dr.NIZET Cécile, CHU LIEGE SITE NOTRE DAME DES BRUYÈRES Rue de Gaillarmont 4032 CHENEE; Dr.HAUWAERT Christian, CHU LIEGE SITE NOTRE DAME DES BRUYÈRES Rue de Gaillarmont 4032 CHENEE; Dr.LUST Catherine, CHU POLYCLINIQUE BRULL Quai Godefroid Kurth 4020 LIEGE; Dr.MARX Linda, PRIVATE PRACTICE Klosterstrasse 4780 ST VITH; Dr.HALLEUX Robert, CH ST VINCENT ST ELISABETH Rue de Naimeux 4802 HEUSY; Dr.SARLET Nathalie, CH ST VINCENT ST ELISABETH Rue de Naimeux 4802 HEUSY; Dr.FONTAINE Marie-Anne, PRIVE Rue Linette 4122 PLAINEVAUX; Dr.HEYLEN Alain, CLINIQUE ST ELISABETH Place Louise Godin 5000 NAMUR; Dr.RONSMANS Isabelle, CLINIQUE ST ELISABETH Place Louise Godin 5000 NAMUR; Dr.DUJARDIN Laurence, PRIVATE PRAC-TICE Avenue Schlogel 5590 CINEY; Dr.MATHY Luc, CH ST VINCENT Rue St Jacques 5500 DINANT; Dr.JEUKENS Thierry, CH BOIS DE L'ABBAYE-HESBAYE Avenue de la Résis-tance 4300 WAREMME; Dr.CORNET Françoise, CH PELZER-TOURELLE Rue du Parc 4800 VERVIERS; Dr.LEFEBVRE Daniel, PRIVATE PRACTICE Place Didier 6700 ARLON; Dr.

PATER Christian, PRIVATE PRACTICE Place Didier 6700 ARLON; Prof.BENTIN Jacques, CENTRE HOSP. UNIVERSITAIRE BRUGMANN Place Arthur Van Gehuchten 1020 BRUXELLES; Dr.FERNANDEZ Maria-Jose, CENTRE HOSP. UNIVERSITAIRE BRUGMANN Place Arthur Van Gehuchten 1020 BRUXELLES; Dr.BADOT Valérie, CENTRE HOSP. UNIVERSITAIRE BRUGMANN Place Arthur Van Gehuchten 1020 BRUXELLES; Dr.SOYFOO Muhammad, HOPITAL ERASME Route de Lennik 1070 BRUXELLES; Dr.MARGAUX Joelle, HOPITAL ERASME Route de Lennik 1070 BRUXELLES; Dr.TANT Laure, HOPITAL ERASME Route de Lennik 1070 BRUXELLES; Dr.DI ROMANA Silvana, HOPITAL UNIVERSITAIRE ST PIERRE Rue des alexiens 1000 BRUXELLES; Prof.DUREZ Patrick, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Prof.HOUSSIAU Frédéric, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Dr. DUFOUR Jean-Pol, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Dr. VANDEN BERGH Marc, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Dr. LAUWERYS Bernard, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Dr. NZEUSSEU Adrien, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Prof.MANICOURT Daniel, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Prof. DEVOGELAER Jean-Pierre, CLINIQUES UNIVERSITAIRES ST LUC Avenue Hippocrate 1200 BRUXELLES; Dr.DOCQUIER Christian, HÔPITAL DE JOLIMONT Rue Ferrer 7100 HAINE-ST-PAUL; Dr. DAUMERIE Florence, HÔPITAL DE JOLIMONT Rue Ferrer 7100 HAINE-ST-PAUL

Author Contributions

Conceptualization: HM RW DE.

Data curation: SDM JL BVDC.

Formal analysis: SDM JL BVDC.

Funding acquisition: RW DE.

Investigation: SDM JL BVDC HM PD RW DE.

Methodology: SDM JL BVDC HM PD RW DE.

Project administration: SDM JL BVDC.

Supervision: HM RW DE.

Writing – original draft: SDM JL.

Writing – review & editing: SDM JL BVDC HM PD RW DE.

References

1. Barton J. Patient preferences and satisfaction in the treatment of rheumatoid arthritis with biological therapy. Patient preference and adherence. 2009; 3:335–44. PMID: 20016797

2. Rau R, Simianer S, van Riel P, van de Putte LBA, Krüger K, Schattenkirchner M, et al. Rapid alleviation of signs and symptoms of rheumatoid arthritis with intravenous or subcutaneous administration of adalimumab in combination with methotrexate. Scandinavian Journal of Rheumatology. 2004; 33(3):145–53. PMID: 15228184

3. Demary W, Schwenke H, Rockwitz K, Kastner P, Liebhaber A, Schoo U, et al. Subcutaneously administered methotrexate for rheumatoid arthritis, by prefilled syringes versus prefilled pens: patient preference and comparison of the self-injection experience. Patient preference and adherence. 2014; 8:1061–71. doi: 10.2147/PPA.S64111 PMID: 25125973

4. Genovese MC, Covarrubias A, Leon G, Mysler E, Keiserman M, Valente R, et al. Subcutaneous abatacept versus intravenous abatacept: a phase IIIb noninferiority study in patients with an inadequate response to methotrexate. Arthritis and rheumatism. 2011; 63(10):2854–64. doi: 10.1002/art.30463 PMID: 21618201

5. Taylor PC, Ritchlin C, Mendelsohn A, Baker D, Kim L, Xu Z, et al. Maintenance of efficacy and safety with subcutaneous golimumab among patients with active rheumatoid arthritis who previously received intravenous golimumab. The Journal of rheumatology. 2011; 38(12):2572–80. doi: 10.3899/jrheum. 110570 PMID: 22089463

6. Burmester GR, Rubbert-Roth A, Cantagrel A, Hall S, Leszczynski P, Feldman D, et al. Efficacy and safety of subcutaneous tocilizumab versus intravenous tocilizumab in combination with traditional DMARDs in patients with RA at week 97 (SUMMACTA). Ann Rheum Dis. 2015.

7. Huynh TK, Ostergaard A, Egsmose C, Madsen OR. Preferences of patients and health professionals for route and frequency of administration of biologic agents in the treatment of rheumatoid arthritis. Patient preference and adherence. 2014; 8:93–9. doi: 10.2147/PPA.S55156 PMID: 24470758

8. Malaviya AP, Ostor AJ. Drug adherence to biologic DMARDS with a special emphasis on the benefits of subcutaneous abatacept. Patient preference and adherence. 2012; 6:589–96. doi: 10.2147/PPA. S23786 PMID: 22936845

9. Jeffery M; Stokes A; Johnson K; Anderson D; Harper B. Patient preferences for tumor necrosis factor (TNF) antagonist administration methods ANNALS OF THE RHEUMATIC DISEASES 2004; 63(Supplement: 1): 510–1.

10. Chilton F, Collett RA. Treatment choices, preferences and decision-making by patients with rheumatoid arthritis. Musculoskeletal care. 2008; 6(1):1–14. doi: 10.1002/msc.110 PMID: 17726671

11. Scarpato S, Antivalle M, Favalli EG, Nacci F, Frigelli S, Bartoli F, et al. Patient preferences in the choice of anti-TNF therapies in rheumatoid arthritis. Results from a questionnaire survey (RIVIERA study). Rheumatology. 2010; 49(2):289–94. doi: 10.1093/rheumatology/kep354 PMID: 19920093

12. Williams EL, Edwards CJ. Patient preferences in choosing anti-TNF therapies-R1. Rheumatology. 2006; 45(12):1575–6. doi: 10.1093/rheumatology/kel369 PMID: 17085468

13. Striesow F, Brandt A. Preference, satisfaction and usability of subcutaneously administered methotrexate for rheumatoid arthritis or psoriatic arthritis: results of a postmarketing surveillance study with a high-concentration formulation. Therapeutic Advances in Musculoskeletal Disease. 2012; 4(1):3–9. doi: 10.1177/1759720X11431004 PMID: 22870490

14. Augustovski F, Beratarrechea A, Irazola V, Rubinstein F, Tesolin P, Gonzalez J, et al. Patient preferences for biologic agents in rheumatoid arthritis: a discrete-choice experiment. Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2013; 16(2):385–93.

15. Fraenkel L, Bogardus ST, Concato J, Felson DT, Wittink DR. Patient preferences for treatment of rheumatoid arthritis. Ann Rheum Dis. 2004; 63(11):1372–8. doi: 10.1136/ard.2003.019422 PMID: 15020312

16. Martin RH, René J, Swartz T, Fiechtner J, Mcintosh B, Holmes-Rovner M. Patient Decision-Making Related to Antirheumatic Drugs in Rheumatoid Arthritis: The Importance of Patient Trust of Physician. The Journal of rheumatology. 2008; 35(4):618–24. PMID: 18278840

17. Zhang J, Xie F, Delzell E, Chen L, Kilgore ML, Yun H, et al. Trends in the use of biologic agents among rheumatoid arthritis patients enrolled in the US medicare program. Arthritis care & research. 2013; 65 (11):1743–51.

18. Smolen J, Landewé R, Breedveld F, Buch M, Burmester G, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2013; 0:1–18.

19. Garneau K, Iversen M, Jan S, Parmar K, Tsao P, Solomon D. Rheumatoid Arthritis Decision Making Many Information Sources but Not All Rated as Useful. Journal Of Clinical Rheumatology 2011; 17 (5):231–5. doi: 10.1097/RHU.0b013e318226a220 PMID: 21778909

20. Willeke P, Becker H, Wassenberg S, Pavenstadt H, Jacobi AM. Patient/rheumatologist evaluation of infusion treatment for rheumatoid arthritis. Zeitschrift fur Rheumatologie. 2011; 70(3):232–4, 6–8. doi: 10.1007/s00393-011-0752-3 PMID: 21359555

21. Curran D, Bacchi M, Schmitz SFH, Molenberghs G, Sylvester RJ. Identifying the types of missingness in quality of life data from clinical trials. Statistics In Medicine 1998; 17(5–7):739–56. PMID: 9549820

22. Joffe M, Rosenbaum P. Invited Commentary: Propensity Scores. Am J Epidemiol. 1999; 150:327–33. PMID: 10453808