Investigation of Patient Satisfaction with Education in a Biosimilar Multiswitch Scenario - A Comparison Between Rheumatologists and Nurse Specialists

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Abstract

The aim of this project was to understand patients' knowledge and opinion about biosimilars and to evaluate patient satisfaction with care after education on multiswitching of biosimilars (bsDMARDs) by rheumatologists in comparison to nurse specialists. Adult patients with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis who underwent a non-medical switch to the adalimumab biosimilar MSB 11022 were randomized into a group in which information about multiswitching of bsDMARDs was provided by a nurse specialist or a rheumatologist. Validated outcome tools and standardized parameters for assessment of disease activity and function were used at baseline and 12 weeks after switching. Patients' satisfaction with care was assessed by the Leeds Satisfaction Questionnaire. A structured questionnaire was used to assess patient's knowledge. A total of 102 patients was randomized, 40 were seen by the rheumatologist (39.2%) and 62 by the nurse (60.8%). Fifty patients (49%) had already undergone one and 52 multiple switches (51%). Less than one third of patients was able to correctly answer questions on manufacturing, effectiveness, clinical trial evidence and cost of bsDMARDs. Patients were generally satisfied with care irrespective of whether the information had been given by the nurse or the rheumatologist. No difference in outcomes was seen.Patient satisfaction and outcomes after education about bsDMARDs and switching by nurses and rheumatologists were similarly good. The number of switches did not have a negative impact on patient satisfaction.

Introduction

Following the approval of the first biosimilar (biosimilar disease modifying anti-rheumatic drug (bsDMARDs)) in the field of rheumatology by the European Comission in 2015, bsDMARDs have captured a steadily growing market [1]. The approval of bsDMARDs is based on totality of the evidence in which efficacy, safety and equivalence to the reference biologic DMARD (bDMARD) has to be demonstrated [2–5]. Although some studies on effectiveness and safety of bsDMARDs in routine care have been published in recent years [6], there is scarcity of data on how patients view and evaluate the use of bsDMARDs – especially in case of multiple switching [7, 8].

Many economic incentives have stimulated the approval of an increasing number of bsDMARDs in the field of rheumatology for, at present, mainly TNF inhibitors (TNFi) and rituximab. As a consequence of the substantial fall of prices, health authorities are often pursuing aggressive strategies for rapid implementation of bsDMARDs for economic reasons. Both internationally and nationally, the proposals range from a non-regulated approach (i.e. the decision making lies solely in the hands of the physician) to rigid guidelines for an obligatory change from reference biologicals to bsDMARDs as in Norway (i.e. the state or the insurance company decides) [8]. Danish data in context of a mandatory switch from reference etanercept to biosimilar SB4 have shown that the retention rate of bsDMARDs was even higher than of non-switchers, even though lower compared to a historical cohort [5–9]. Patient factors and non-specific drug effects may have had an impact on retention rates [10].

In Germany, the national authorities ‘Paul-Ehrlich Institut’ [11] and ‘Arzneimittelkom-mission der deutschen Ärzteschaft’ [12] have taken very clear positive positions on the use of bsDMARDs in clinical practice. However, on the German national level the prescription of bsDMARDs has been differently handled in regional associations of panel physicians (KV). For example, in our area, Westfalen-Lippe, rheumatologists are confronted with a requirement of a biosimilar quota of >90% - which practically means that almost all patients have to be started on a biosimilar, and an existing therapy with a reference biologic agent has to be switched to a biosimilar. In consequence, multiple switches also between bsDMARDs are to be expected. Such multiswitch scenarios occur because of economic factors but also due to loss of efficacy and potential side effects of the previous biosimilar [13]. As recently shown by our group and others [14] multiswitching did not affect disease activity over a 6-month observational period suggesting that it is safe and effective [15]. However, in other open-label studies in which all patients in remission were automatically switched to bsDMARDs, the retention rate was low [16]. In anecdotal case reports loss of efficacy after switching has been described [17].

The patients’ view on bsDMARDs and multiswitching of bsDMARDs has not been well investigated to date [20]. Lack of acceptance and negative perceptions about bsDMARDs may lead to increased nocebo effects [6] after a change of therapy and potentially compromise patient compliance [21]. Studies have shown that some patients have a negative perception on bsDMARDs and may not even be willing to switch medication at all [20]. Negative perceptions include beliefs that bsDMARDs are inferior in quality, safety and efficacy compared to the reference product. International and national recommendations have included patient education in general and the efficacy and safety of nurse led programs in particular [19, 22]. Patient guidance by specialised nurses in an outpatient setting has been shown to be effective and safe and that the performance of such nurses are equivalent to rheumatologists including physical examination [23]. Importantly, patients' need to be well trained about their illness and the necessary therapies. The educational process may be covered by nurse specialists which even led to improved patient satisfaction [24]. Our experience with biologics goes back to the beginning of the millennium [25], and bsDMARDs have been used in our center ever since their first approval in rheumatology in 2015. Accordingly, adalimumab bsDMARDs have been used since October 2018. Furthermore, well trained nurse specialists have been working in our center for several years.

The objectives of this project was (I) to investigate patients’ knowledge and opinion on bsDMARDs, (II) to explore the impact of multiple switches on patient satisfaction, and (III) to evaluate whether satisfaction with care differ when receiving education about a bsDMARD to bsDMARDs adalimumab switch from a rheumatologist or nurse specialists.in patients with chronic inflammatory rheumatic diseases (CIRD) treated in routine care.

Material And Methods

Population: Adult patients diagnosed with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA) who had been treated with an adalimumab biosimilar, were planned to be switched to the adalimumab biosimilar MSB 11022. All patients who fulfilled this inclusion criteria were

invited to participate and gave informed consent for the study. Patients who did not have appropriate language skills could not participate in this study.

A non-medical switch from adalimumab biosimilar GP2017 to the adalimumab biosimilar MSB 11022 was used as an opportunity to study patients' knowledge, their view on bsDMARDs and their satisfaction with the educational process longitudinally. Patients were stratified on having experienced the first switch from first to second adalimumab bsDMARD (mono-switch) or to >1 switch between different adalimumab bsDMARDs in the past (multi-switch).

Study design

Patients were 1:1 randomized into two groups by means of block randomisation with a variable length of blocks (block was defined as one month): Information provided by the rheumatologically trained nurse specialist (nurse led care (NLC)), and information provided by the rheumatologist (rheumatologist led care (RLC)). study visit at baseline and week 12 during the routine visit in the outpatient clinic. The primary endpoint was to evaluate differences in patient satisfaction after education about a bsDMARD to bsDMARDs adalimumab switch between rheumatologists and nurse specialists. The secondary endpoint was to identify the outcome of mono- and multi-switching scenarios in routine care with respect to patients’ attitudes towards bsDMARDs. The study was approved by the Ethical Committee of the Ruhr-Universität Bochum, Germany (Registration number 20-6990). Written informed consent was obtained from all participants.

Educational process

Four rheumatologists and 2 nurse specialists provided standardized information on the switch to another bsDMARD based on the information strategy provided in routine care. Information process was supported by standardized leaflets about different drug treatments provided by the German Society of Rheumatology. In Germany, nurse specialists have completed a standardized curriculum and successfully passed a final examination also on drug therapy. In addition, the nurse specialists in our study were educated about bsDMARDs once more directly before the start of the study. Patients received the education session directly after the visit by the treating rheumatologists and were followed up for 12 weeks.

Outcome measures

Patients filled in paper-based package of study questions during their time in the outpatient clinic. At baseline, patients filled out the study documents before the education session. Demographics and clinical data including comorbidities, laboratory parameters (rheumatoid factor, HLA-B27, C-reactive protein (CRP)) and concomitant medication were documented at the baseline visit which was defined by

the day of the switch to adalimumab biosimilar MSB 11022. Disease activity was assessed in RA and PsA patients by the 28-joint Disease Activity Score (DAS28) [27], and in axSpA patients by the Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI) and the AS Disease Activity Score (ASDAS) [28]. Physical function was assessed in RA and PsA patients by using the Funktionsfragebogen Hannover (FFbH) score, which correlates well with the Health Assessment Questionnaire (HAQ). Values of FFbH were converted into HAQ values by the formula: HAQ score = 3.16 – (0.028 × FFbH score) [29]. In axSpA patients, physical function was assessed by the Bath AS functional index (BASFI) [30]. Demographic and clinical data as well as assessment of disease activity and physical function as well as biosimilar tolerance, safety and adherence were taken from hospital notes documented at the baseline and follow-up visit at 12 weeks.

In addition to standard care, a structured questionnaire was used at baseline to assess patients' perceived knowledge about manufacturing, effectiveness, acceptance, evidence from clinical trials and costs of bsDMARDs, as well as sources of information about bsDMARDs. In addition, we asked all patients whether the information about bsDMARD was understandable. The structured questionnaire contained 1 closed question, 2 questions with a NRS (1-10) and 5 questions with multiple response options plus free text. These questions refer to manufacturing, effectiveness, acceptance and costs. Satisfaction with care was assessed by the standardized Patient Satisfaction Questionnaire (PSQ) at baseline and 12 weeks [26]. The questionnaire contains items on five subscales: information, empathy with and attitude to the patient, access to and continuity with the healthcare provider, technical competence and a general satisfaction scale. Patients were asked to indicate their level of agreement to 45 statements by responding to a 5-point Likert scale (range between strongly agree (1) to strongly disagree (5). Scores 3 indicate ≥ satisfaction and < 3 dissatisfaction.

Statistical Analyses

Descriptive statistics are presented as absolute frequencies and percentages when referring to qualitative variables. Continuous variables were expressed as mean values and standard deviations. A value of $p < 0.05$ was considered statistically significant. Pearson's Chi-squared tests to compare groups were performed using SPSS, version 26.

Results

Characteristics of the study population

124 patients were invited to participate, and 102 were enrolled into the study (figure 1). Main reason for refusal was personal reasons to decline participation or low language skills. Irrespective of study participation, all patients were switched to adalimumab MSB 11022. 62 (60.8%) patients were randomized to NLC and 40 (30,2%) to RLC. There were 26 (25.4%) patients with RA, 61 (59.8%) with axSpA and 15 (14.8%) with PsA (Table 1). 56 (52.8%) were male, mean age 48.7 years (13.6), mean CRP

0.2 mg/dl (0.33), with 12 (11.7%) having an elevated CRP (cut-off 0.5 mg/dl).A total of 50 patients had already undergone one (49%) and 52 (51%) multiple switches. Patients were in moderate to low disease activity states and had some impairments in physical function (Table 2). Patients in both groups did not differ between baseline characteristics.

Table 1
Patients and disease characteristics in both groups

Variables *	**Total group**	**NLC (n=62)**	**RLC (n=40)**	**P-Value#**
Sex, male, n (%)	56 (54.9%)	31 (50%)	25 (62.5%)	0.215
Age, years	48.7(13.5)	48.8 (13.9)	48.7 (13.3)	0.996
Rheumatoid Arthritis, n (%)	26 (25.5)	16 (25.8%)	10 (25%)	0.927
Axial Spondyloarthritis, n (%)	61 (59.8%)	36 (58.1%)	25 (62.5%)	0.656
Psoriatic arthritis, n (%)	15 (14.8%)	10 (16.1%)	5 (12.5%)	0.613
Disease Duration, years	9.8 (9.4)	9.4 (10,9)	10.5 (9,2)	0.574
Number of previous bDMARDs	1.4 (0.9)	1.5 (0.7)	1.4 (1)	0.452
DAS28	2(1.1)	1.4(1.1)	2.5(0.9)	0.003
HAQ	1(0.8)	0.9(0.7)	1.1(0.4)	0.254
BASFI	3.5(2.7)	3.2/2.7)	3.8(2.5)	0.397
ASDAS	2.1(1)	1.9(1)	2.2(0.9)	0.294
Comprehensibility of the information	7(3.1)	8(3.2)	7(3.1)	0.450
Concerns regarding the switch	3(2.7)	2.5(2.5)	3(2.8)	0.294
* values are mean (SD); # between NLC and RLC				
NLC = nurse led clinic ; RLC = rheumatologist led clinic				

Table 2
Change of disease activity and physical function in both groups during follow-up

Assessments*	NLC			RLC			
	Baseline	Follow-up	Difference Follow-up – Baseline	Baseline	Follow-up	Difference Follow-up – Baseline	P – Value#
DAS28	2.0 (0.9)	2.4 (0.9)	0.2 (0.7)	1.3 (1)	1.3 (0.8)	0.2 (0.7)	0.006
HAQ	0.9 (0.7)	1.1 (0.5)	0.08 (0.3)	1.1 (0.4)	0.8 (0.6)	0.1 (0.4)	0.224
BASFI	3.3 (2.7)	2.9 (2.5)	0.3 (0.9)	3.9 (2.5)	3.6 (2.6)	0.3 (1.7)	0.526
ASDAS	1.9 (1)	1.9 (0.8)	0.1 (0.7)	2.1 (0.9)	2 (0.8)	0.01 (0.5)	0.271
* values are mean (SD); #p-value comparing differences between NLC and RLC							
NLC = nurse led clinic ; RLC = rheumatologist led clinic							
NLC = nurse led clinic ; RLC = rheumatologist led clinic ;							
LSQ = Leeds Satisfaction Questionnaire							

At follow up, 98 patients were analysed. Four patients were lost to follow up. The remaining other patients adhered adalimumab MSB 11022. 59 patients were evaluated in the NLC group and 39 in the RLC group at the control visit (Figure 3.). Scores of disease activity and physical function during follow-up remained unchanged (Table 2).

Perceived knowledge about bsDMARDs and information needs

Less than one third of patients was able to correctly answer questions before the education about manufacturing, effectiveness, acceptance and costs of bsDMARDs (Figure 1). Almost 75% of the patients had no concerns to be switched to a new bsDMARD (quotation from free text box: “I do not notice any difference”). The majority of patients expected the same effectiveness (75%) and safety (60%) of bsDMARDs compared to the previous bsDMARD. The main sources of information about bsDMARDs were rheumatologists and nurses (78%), the internet (36%) and patient associations (5%). Only, 12% of the patients indicated that information about bsDMARD was understandable (quotation from free text box: “much was explained, little was understood”).Knowledge about bsDMARDs did not differ between patients who already underwent multiple bs – to bsDMARD switches compared to patients who received the first bsDMARD to bsDMARD switch.

Patient satisfaction regarding the educational process

Patients were generally satisfied with care irrespective of whether information about bsDMARDs and switching had been given by the nurse or the rheumatologist (Table 2). Subdomains were not rated differently by patients. Multiswitching did not lead to reduced satisfaction with care in patients on bsDMARDs, and the number of switches did not have a negative impact on patients' satisfaction (Figure 2). The vast majority (95%) of patients who had undergone multiple switches were satisfied with the ongoing therapy.

Discussion

This study shows that the satisfaction and outcomes of patients educated about bsDMARDs by nurse specialists were not different from the information provided by rheumatologists. Multiswitching did not lead to reduced satisfaction with care in patients on bsDMARDs and the number of switches did neither have a negative impact on patients' satisfaction nor on disease activity or physical function of patients. However, patients' knowledge on bsDMARDs was limited. Furthermore, the study shows that the information on bsDMARDs provided by nurse specialists was as good as that given by the rheumatologist [31–32]. This is largely consistent with data of a British multicentre study, in which the overall satisfaction with rheumatologic care was higher when nurse specialists provided the information on the treatment process [3, 5, 24, 26]. As recommended by EULAR [6] patients should have access to nurse consultations in order to enhance satisfaction with care', and this is based on the overarching principle 'Rheumatology nursing is based on the principles of evidence-based practice". Indeed, there is evidence that patient information provided by nurse specialists leads to improved self-management skills, increased self-efficacy and global well-being in patients with RA [37]. Thus, information on bsDMARDs can and should be provided by nurse specialists. However, the situation described here is different from a shared decision making process with an open end since the decision to switch was already made when patients were informed about it. Moreover, there is a lack of data concerning a bsDMARD-to-bsDMARD transition. Thus, our findings cannot be generalized.

Our study shows that patient information on bsDMARDs may not be optimal because less than one third of patients was able to correctly answer questions on bsDMARDs. Is it possible and is it needed to further increase patients' knowledge ? Theoretically, we clearly think: yes. However, patients may have major differences in their educational status [38]. Even though not assessed in this study, such differences and educational inequalities may well have influenced the results of this study. In this regard, it seems appropriate to mention the Educational Needs Assessment Tool (ENAT) that is used to identify and prioritise patients' individual educational needs [39]. The ENAT has indeed been shown to significantly increase the effect of patient education delivered by nurses. Another approach just recently reported is to implement educational interviews by pharmacists on knowledge and adherence to biologics [40] which significantly increased patients' knowledge scores on therapy with biologics. It has been shown that positive framing can improve perceptions of and willingness to switch to a biosimilar in patients currently taking bDMARDs [41]. However, even though being well aware of this issue, we didn't pay much attention

to this important aspect when informing patients about bsDMARDs in this study. Nevertheless, since we have been discussing this intensively in our team [21] we cannot exclude that the rheumatologist and the nurse who provided the information on bsDMARDs has taken advantage of positive framing. One smaller study indicated that possible nocebo effects may be reduced by a tailored communication with a prominent role of nurses [42]. Finally, not only switching but also not multiswitching seemed to be a major problem for patients with CIRD which is consistent with an early controlled study on multiswitching [43] and our data on the lack of nocebo effects in patients switched from originator to a biosimilar [44]. However, it has been reported that more than a few patients switch back to the originator [44]. Nevertheless, in this study most patients switched from biosimilar to biosimilar which implies that they were not naïve to the use of bsDMARDs.

This study also has some limitations. First, the study design was retrospective which implies that unknown factors which could not been controlled for may have biased the results. Second, our population was mixed in two ways: some patients had already experienced switches, other not, and, of course, there were three different types of diagnosis involved: RA, axSpA and PsA which brings some heterogeneity in. Third, we did not systematically check which other sources of information the patients had used. Finally, we cannot exclude that the pandemic had an influence on results.

Taken together, the main result of this study is that nurse specialists are at least equally capable of providing information on bsDMARDs compared to rheumatologists. It is likely that this can even be improved by specialized training and more education on framing and nocebo effects. Multiswitching does not seem to be a major problem but this may not be the case for all patients. Appropriate patient information and education is mandatory to achieve good clinical results. Shared decision making is, in the area of non-medical switching and treatment decisions following economic principles, a difficult task but patient information and education becomes then even more important.

Declarations

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References

1. Probiosimilar.de [Internet]. Berlin: What is a biosimilar ? [Update May 2016, cited July [2021] Available from: https://probsDMARDs.de
2. Park W, Yoo DH, Miranda P et al. Efficacy and safety of switching from reference infliximab to CT-P13 compared with maintenance of CT-P13 in ankylosing spondylitis: 102-week data from the PLANETAS extension study. Ann Rheum Dis 76: 346–354.
3. Emery P, Vencovský J, Sylwestrzak A et al. A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy. Ann Rheum Dis 76: 51–57.
4. Weinblatt ME, Baranauskaite A, Dokoupilova E et al. Switching From Reference Adalimumab to SB5 (Adalimumab Biosimilar) in Patients With Rheumatoid Arthritis: Fifty-Two-Week Phase III Randomized Study Results. Arthritis Rheumatol 70: 832–840.
5. Edwards CJ, Monnet J, Ullmann M et al. Safety of adalimumab biosimilar MSB11022 (acetate-buffered formulation) in patients with moderately-to-severely active rheumatoid arthritis. Clin Rheumatol 38: 3381–3390.
6. Kiltz U, Pudelko JC, Tsiami S, Baraliakos X, Braun J. Non-medical switching from reference to biosimilar etanercept - no evidence for nocebo effect: a retrospective analysis of real-life data. Clin Exp Rheumatol. 2021 Jan 7. Epub ahead of print.
7. Barbosa CM, Rodríguez de Castro B, Labeaga Beramendi Y, et. al. Patient satisfaction survey: substitution of reference etanercept with a biosimilar product. Eur J Hosp Pharm. 2021 Mar;28(2):109-111.
8. Peyrin-Biroulet, L., Lönnfors, S., Avedano, L. and Danese, S. (2019), Changes in inflammatory bowel disease patients' perspectives on biosimilars: A follow-up survey. UEG Journal, 7: 1345-1352
9. Bech B, Primdahl J, van Tubergen A, Voshaar M, Zangi HA, Barbosa L, et al.. 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. Ann Rheum Dis 2020 Jan;79(1): 61-68. Epub 2019 Jul 12.
10. Glintborg B, Loft AG, Omerovic E et al. To switch or not to switch: results of a nationwide guideline of mandatory switching from originator to biosimilar etanercept. One-year treatment outcomes in 2061 patients with inflammatory arthritis from the DANBIO registry. Ann Rheum Dis 78: 192–200.
11. Pei.de [Internet] Berlin: Position des Paul-Ehrlich-Instituts zum Einsatz von BsDMARDs [Update 2019 November 21, cited 2021 July 4]. Avalaible from : http://www.pei.de

12. akdae.de [Internet] Münster : Leitfaden "BsDMARDs",2.Auflage [Update January 2021, cited July 2021]. Available from http://www.akdae.de
13. Edelaar L, Nikiphorou E, Fragoulis GE, Iagnocco A, Haines C, Bakkers M, et al.. 2019 EULAR recommendations for the generic core competences of health professionals in rheumatology. Ann Rheum Dis 2020 Jan;79(1): 53-60. Epub 2019 Aug 9.
14. Feagan, B.G., Marabani, M., Wu, J.J. *et al.* The Challenges of Switching Therapies in an Evolving Multiple BsDMARDs Landscape: A Narrative Review of Current Evidence. *Adv Ther* **37,** 4491–4518 (2020).
15. Kiltz U, Tsiami S, Baraliakos X et al. AB1171 Effects of successive switches of two different bsDMARDs of etanercept on outcomes in inflammatory rheumatic diseases in daily practice. Ann Rheum Dis 79: 1876.
16. Avouac J, Moltó A, Abitbol V, et al. Systematic switch from innovator infliximab to biosimilar infliximab in inflammatory chronic diseases in daily clinical practice: The experience of Cochin University Hospital, Paris, France. Semin Arthritis Rheum 2018;47:741–8.
17. Cantini F, Niccoli L, Nannini C, et al. Rapid loss of efficacy of biosimilar infliximab in three patients with Behçet's disease after switching from infliximab originator. Eur J Rheumatol 2017;4:288–90.
18. Patermann J, Ehlebracht-König I, Lind-Albrecht G, Genth E, Reusch A, Küffner R, et. al. EULAR-Empfehlungen für die Schulung von Patienten mit entzündlich-rheumatischen Gelenkerkrankungen. Übersetzung und Bewertung für Deutschland [EULAR recommendations for patient education of people with inflammatory arthritis. Translation and evaluation in Germany]. Z Rheumatol. 2016 Mar;75(2):187-99.
19. Sarnola K, Merikoski M, Jyrkkä J et al. Physicians\textquoteright perceptions of the uptake of bsDMARDs: a systematic review. BMJ Open 10.
20. Gasteiger C, Lobo M, Dalbeth N et al. Patients' beliefs and behaviours are associated with perceptions of safety and concerns in a hypothetical biosimilar switch. Rheumatology international.
21. Braun J, Tsiami S, Buehring B, Kiefer D, Andreica I, Baraliakos X, et al. BsDMARDs und der Nocebo-Effekt [BsDMARDs and the nocebo effect]. Z Rheumatol 2020 Apr;79(3):267-275.
22. Krause A, Schuch F, Braun J, Gauler G, Hoeper K, Krüger K, et al. Delegation ärztlicher Leistungen in der Rheumatologie [Delegation of medical tasks in rheumatology]. Z Rheumatol 2020 Mar; 79(2): 123-131
23. Kiltz U, Spiller I, Sieper J et al. Is it possible to delegate medical services to qualified nurses specialized in rheumatology when evaluating patients with suspicion of ankylosing spondylitis?-Results of the PredAS study (Ist eine Delegation ärztlicher Leistungen auf rheumatologische Fachassistenten bei der Evaluierung von Patienten mit Verdacht auf ankylosierende Spondylitis möglich? – Ergebnisse der PredAS-Studie). Z Rheumatol 79: 729–736.
24. Hill J, Bird HA, Hopkins R et al. Survey of satisfaction with care in a rheumatology outpatient clinic. Ann Rheum Dis 51: 195–197.

25. Braun J, Sieper J. Ankylosing spondylitis. Lancet. 2007 Apr 21;369(9570):1379-1390. doi: 10.1016/S0140-6736(07)60635-7. PMID: 17448825.
26. Ndosi M, Lewis M, Hale C et al. The outcome and cost-effectiveness of nurse-led care in people with rheumatoid arthritis: a multicentre randomised controlled trial. Ann Rheum Dis 73: 1975–1982.
27. van der Heijde, D M, van 't Hof, M A, van Riel PL et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis 49: 916–920.
28. Garrett S, Jenkinson T, Kennedy LG et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 21: 2286–2291
29. Lautenschläger J, Mau W, Kohlmann T et al. Comparative evaluation of a German version of the Health Assessment Questionnaire and the Hannover Functional Capacity Questionnaire (Vergleichende Evaluation einer deutschen Version des Health Assessment Questionnaires (HAQ) und des Funktionsfragebogens Hannover (FFbH)). Z Rheumatol 56: 144–155.
30. Calin A, Garrett S, Whitelock H et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 21: 2281–2285
31. Germain V et al. (2018) Long-term follow-up after switching from originator infliximab to its biosimilar CT-P13: the weight of nocebo effect. Ann Rheum Dis 2018;0:1–2. doi:10.1136/annrheumdis-2018-21437
32. Fleischmann R, Jairath V, Mysler E, Nicholls D, Declerck P. Nonmedical Switching From Originators to BsDMARDs: Does the Nocebo Effect Explain Treatment Failures and Adverse Events in Rheumatology and Gastroenterology? Rheumatology and Therapy. 2020 Mar;7(1):35-64.
33. Smolen JS, Landewé RBM, Bijlsma JWJ, Burmester GR, Dougados M, Kerschbaumer A et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis. 2020 Jun;79(6):685-699. Epub 2020 Jan 22
34. van der Heijde D, Ramiro S, Landewé R*, et al.*2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis Annals of the Rheumatic Diseases 2017;76:978-991.
35. Gossec L, Baraliakos X, Kerschbaumer A*, et al.* EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Annals of the Rheumatic Diseases 2020;79:700-712.
36. Stacey D, Légaré F, Lewis K, Barry MJ, Bennett CL, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev 2017 Apr 12;4(4):CD001431.
37. Dy SM, Purnell TS. Key concepts relevant to quality of complex and shared decision-making in health care: a literature review. Soc Sci Med. 2012 Feb;74(4):582-7. Epub 2011 Dec 23.
38. Kiadaliri AA, Petersson IF, Englund M. Educational inequalities in mortality associated with rheumatoid arthritis and other musculoskeletal disorders in Sweden. BMC Musculoskelet Disord. 2019 Feb 18;20(1):83.

39. Ndosi M, Johnson D, Young T, Hardware B, Hill J, Hale C, et al. Effects of needs-based patient education on self-efficacy and health outcomes in people with rheumatoid arthritis: a multicentre, single blind, randomised controlled trial. Ann Rheum Dis. 2016 Jun;75(6):1126-32. Epub 2015 Jul 10.
40. Gutermann L, Dumas S, Lopez-Medina C, Boissinot L, Cotteret C, Perut V, Molto A, Conort O, Dougados M. Impact of a pharmacist-led programme on biologics knowledge and adherence in patients with spondyloarthritis. Clin Exp Rheumatol. 2021 Jul-Aug; 39(4):811-818. Epub 2020 Oct 9.
41. Gasteiger C, Jones ASK, Kleinstäuber M, Lobo M, Horne R, Dalbeth N, et al. Effects of Message Framing on Patients' Perceptions and Willingness to Change to a Biosimilar in a Hypothetical Drug Switch. Arthritis Care Res (Hoboken) 2020 Sep; 72(9):1323-1330. Epub 2020 Jul 23.
42. Petit J, Antignac M, Poilverd RM, Baratto R, Darthout S, Desouches S, Louati K, et.al. Multidisciplinary team intervention to reduce the nocebo effect when switching from the originator infliximab to a biosimilar. RMD Open. 2021 Jan;7(1):e001396.
43. Griffiths CEM, Thaçi D, Gerdes S, Arenberger P, Pulka G, Kingo K, et.al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. Br J Dermatol 2017 Apr;176(4):928-938. Epub 2017 Mar 1.
44. Reuber K, Kostev K. Prevalence of switching from two anti-TNF bsDMARDs back to biologic reference products in Germany. Int J Clin Pharmacol Ther. 2019 Jun;57(6):323-328.

Figures

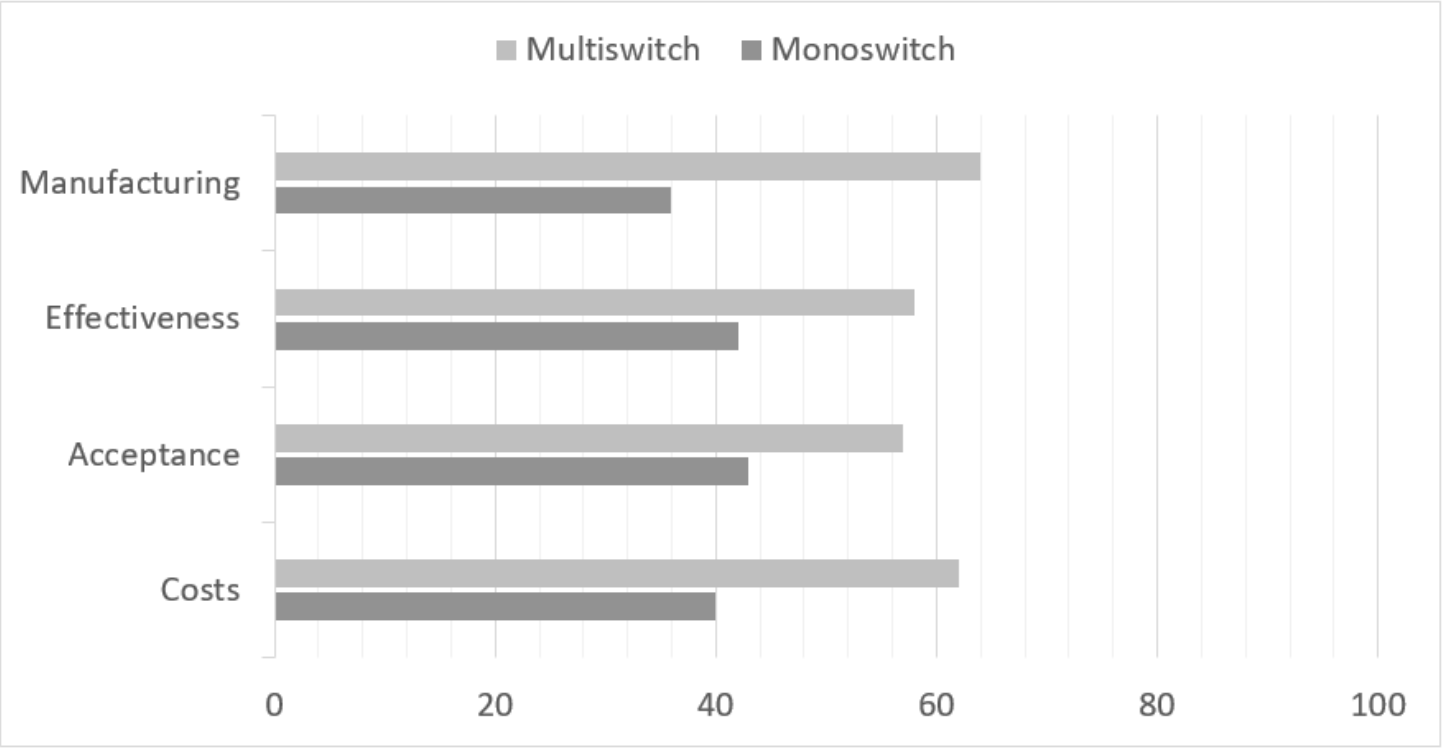

Figure 1

Patients’ knowledge about bsDMARDs

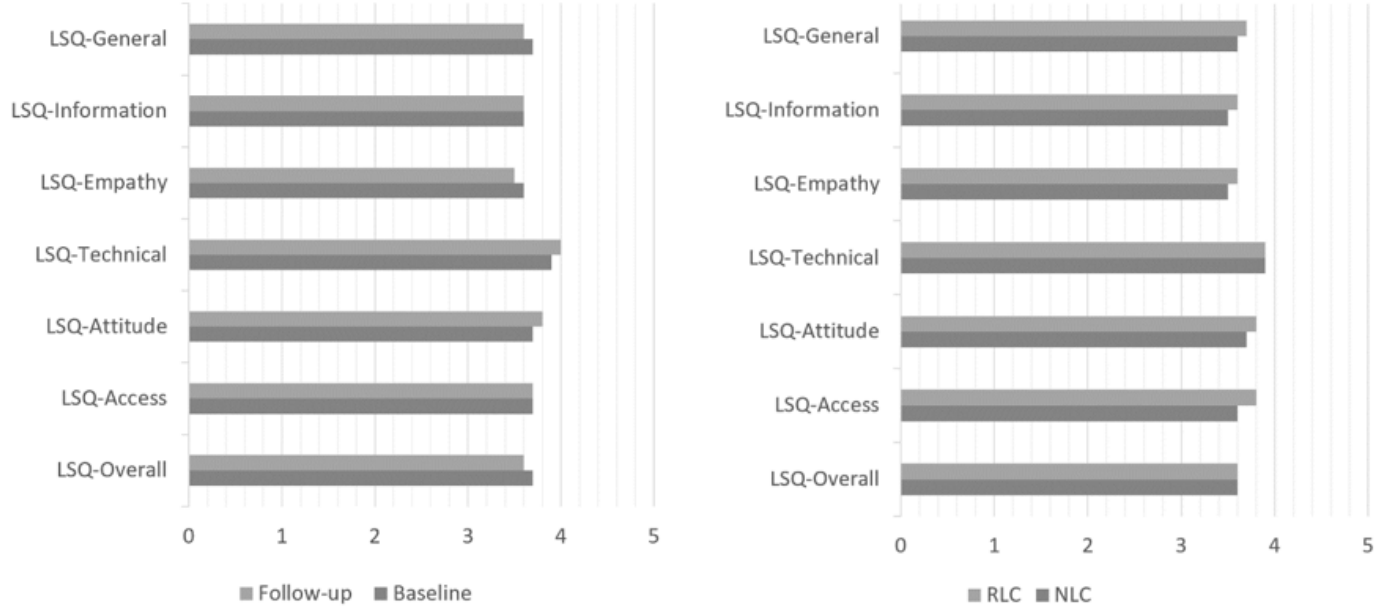

Figure 2

Satisfaction of patients who were educated by a nurse specialist (NLC) or a rheumatologist (RLC) at baseline and at follow-up

NLC = nurse led clinic ; RLC = rheumatologist led clinic ;

LSQ = Leeds Satisfaction Questionnaire

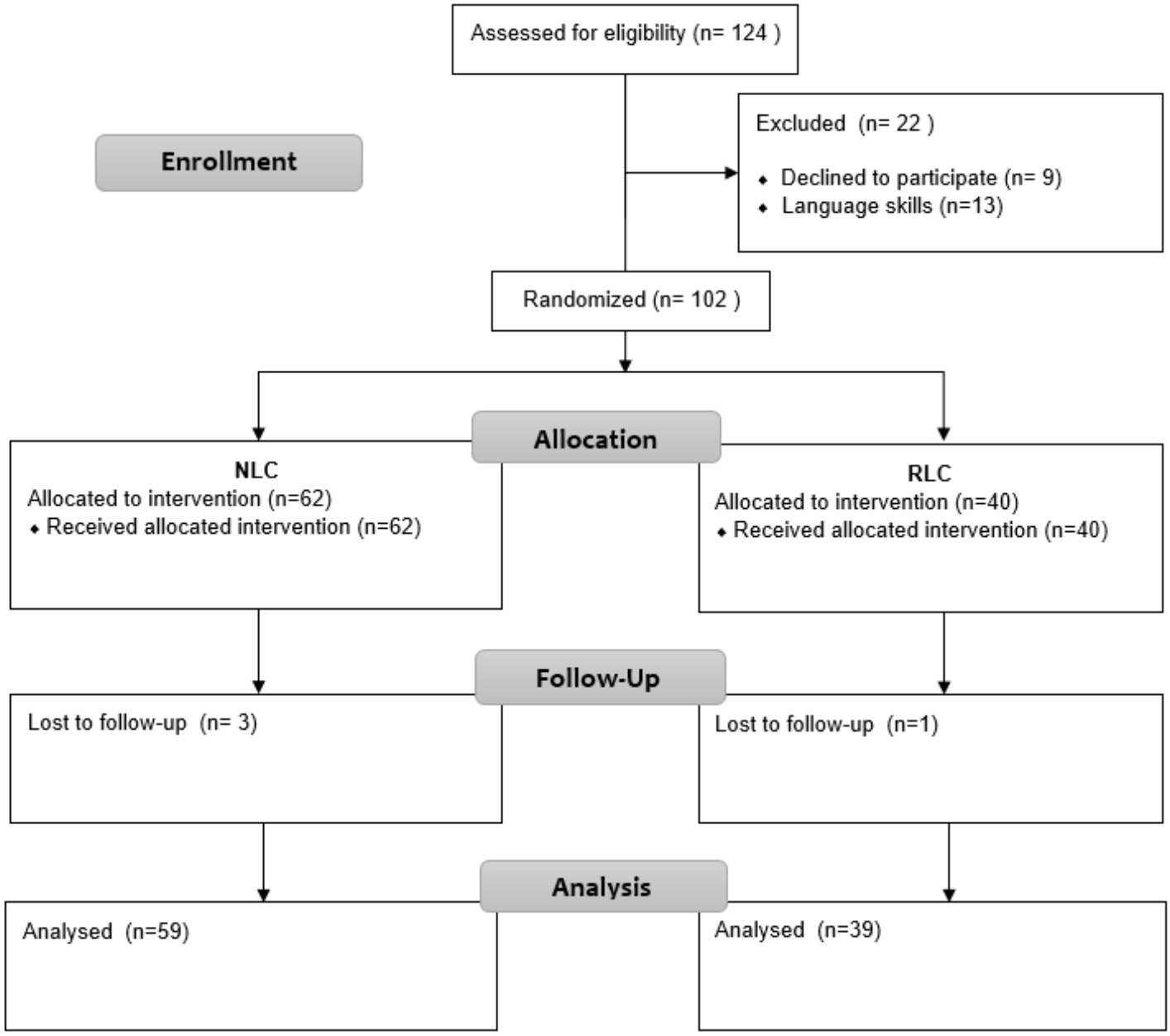

Figure 3

Consort 2010 Flow Diagramm