Rheumatol. Forum
2023, vol. 9, No. 3, 140–144

ISSN: 2720-3921, e-ISSN: 2720-3913
DOI: 10.5603/RF.a2023.0011

VIA MEDICA
www.journals.viamedica.pl

REVIEW ARTICLE

Marta Jeka[1], Daniel Jeka[2], Eugeniusz Daniszewski[3], Ewa Mojs[4]

[1]Medicover Integrated Clinical Services, Warszawa, Poland
[2]Innovative Therapies Clinic, Torun, Poland
[3]Medicover — Nasz Lekarz, Torun, Poland
[4]Department of Clinical Psychology, Poznan University of Medical Sciences, Poznan, Poland

Psychodemographic characteristics of patients with rheumatic diseases in clinical trials: Preliminary findings

ABSTRACT

Introduction: Clinical trials are an integral part of medical progress. Today, it would be difficult to imagine modern medicine without them. Clinical trials make it possible not only to assess the efficacy of new therapies but also their safety profile. Unfortunately, the increase in complexity of clinical trial protocols that have been observed in recent decades makes patient recruitment for clinical trials increasingly difficult. Patients not only have to meet strictly defined inclusion and exclusion criteria but also have to adapt their daily lives to the requirements of clinical trials.
Aim: This study aims to develop psychodemographic characteristics of patients with rheumatic diseases who had completed at least one clinical trial.
Material and methods: Sixty-nine (50K/19M) patients with rheumatic diseases were included in the study. The mean age of patients included in the study was 50.8 ± 12.9 years and the mean duration of disease was 13.1 ± 9.3 years. The inclusion criterion for the study was the completion of at least one clinical trial. Patients enrolled in the study completed **a** questionnaire in which questions covered demographic data, subjective assessment of financial status and health status, and reasons for participating in the clinical trial.
Results: Patients participating in clinical trials include 66.5% of those with a secondary or higher education. Fifty-nine percent of patients rate their financial status as average and 61% of patients are economically active. Eighty-nine percent of patients rate their health status as poor or very poor before entering the clinical trial.
Conclusions: Patients participating in clinical trials are generally those with long disease duration, poor health status and a financial status that does not allow them to buy biologics.

Rheumatol. Forum 2023, vol. 9, No. 3: 140–144

KEY WORDS: clinical trials; rheumatoid arthritis; psoriatic arthritis; systemic lupus erythematosus; rheumatic diseases

INTRODUCTION

Modern medicine is developing much more rapidly than it did in the past. However, many diseases still require the introduction of new therapies to effectively treat patients. Therefore, it is necessary to continue scientific research into new therapies and, as a result, also conduct clinical trials. Clinical trials can be considered as a bridge between science and routine medical practice. Their aim is to both assess the efficacy and safety of new therapies.

Currently, the top priority in clinical trials is to protect the rights of each study participant — to ensure safety. The regulations are defined by the 1964 Declaration of Helsinki and, in the case of clinical trials, Good Clinical Practice (GCP) is the basis.

Clinical trials aim to produce reliable data so that drugs that are both effective and have a very high safety profile can be brought to

Address for correspondence:
Marta Jeka, MBA
Medicover Integrated Clinical Services
Wronia 53/B10
00–874 Warszawa, Poland
e-mail: jeka10@wp.pl

market. Regulations in this area are governed by the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) in Europe and the United States, respectively.

In previous decades, clinical trials were not always conducted according to ethical principles. Currently, clinical trial protocols are much more rigorous and great emphasis is placed on patient safety. Before this change, many myths about clinical trials emerged, which can still divide and electrify the public opinion today.

Unfortunately, the bad reputation of clinical trials is not without a real basis. In the history of medicine, drugs such as rofecoxib (Vioxx) or thalidomide have left a bad mark [1, 2]. It is also worth recalling the recent history of the AIDS drug trial in New York, which sparked controversy even within the medical community [3, 4].

Thalidomide, which causes phocomelia, was a drug marketed in a completely different era. The 1950s and 1960s in terms of scientific research methodology significantly differed from today's standards.

However, rofecoxib is no longer such a distant history. In a way, rofecoxib shows how the analysis of research results can be difficult — even for specialists. It would seem that the statistical analysis is a tool that provides a very objective assessment of the data. In reality, it turned out to be quite the opposite. The research findings, including the safety profile of the drug, were published in one of the most prestigious journals in the medical field — "New England Journal of Medicine" [6]. The story of this publication has shown that even the best reviewers cannot guard against mistakes. In addition to editors and reviewers, for a certain period of time even readers failed to catch some inconsistency in the conducted analysis [6].

It should be noted that rofecoxib was also used in patients with rheumatoid arthritis (RA). Before rofecoxib was withdrawn from the market, there were even published findings indicating that not only was it more effective than placebo but also its safety profile was similar to placebo [7].

The Internet, which is now the first source of knowledge for patients, is home to many such stories. Some of them, like those presented above, may be true but others have more in common with science fiction than truth.

From a scientific perspective, the stories discussed above are fortunately the infamous exceptions. Hundreds of clinical trials are currently underway around the world, which are conducted with integrity i.e., respecting ethics, legal standards, and modern scientific methodology. Naturally, well-conducted clinical trials do not generate much interest from the media.

However, the current problem of finding patients who are willing to participate in clinical trials is not only related to the bad reputation of clinical trials. Paradoxically, difficulties in recruiting patients also result from the previously taken remedial steps, which have led to minimising stories like the three mentioned above.

Over the past two decades, there has been an unprecedented increase in the complexity of protocols in the history of clinical trials [8]. Changes to clinical trial protocols resulted in two major consequences. First and foremost, the cost of conducting clinical trials has increased. A second, much more serious effect that has a measurable impact on patient recruitment is the increased duration of clinical trials [8].

The process of including a patient in a trial is time-consuming – both from the perspective of the potential patient and the researcher. Moreover, patients usually have to meet very strict inclusion and exclusion criteria. For this reason, increasing importance is being placed not only on finding patients who meet all the criteria but also on finding patients who will not drop out of the clinical trial within a few months.

Modern trial protocols are highly demanding for patients. They heavily interfere with their lifestyle — for example, through frequent visits to the doctor or the need to spend several hours at the centre to complete all the procedures required by the trial protocol. For this reason, there is an increasing emphasis on patient education aimed at encouraging patients to participate in clinical trials. The problem of patient recruitment is so serious that both the EMA and the FDA have begun to promote clinical trials to potential participants [8].

In addition, a psychological profile of the average clinical trial participant can also be attempted. This makes it possible to identify a group of patients who are very likely to be interested in participating in clinical trials and will not drop out during the course of the trial.

AIM

This study aims to try to establish the profile of patients with rheumatic diseases who would agree to participate in a clinical trial — therapy with biologics, the availability of which is still limited in Poland.

Table 1. Demographics of the study group by sex

	Entire group
Number of patients [n]	69 (50K/19M)
Average age [years] (± SD; median; min.; max.)	50.8 (± 12.9; 51; 23; 74)
BMI [kg/m^2] (± SD; median; min.; max.)	27 (± 5; 26; 20; 39)
Number of patients with BMI ≥ 25 [n] (%)	43 (62%)
Average duration of disease [years] (± SD; median; min.; max.)	13.1 (± 9.3; 10; 1; 40)

Source: authors' own study; BMI — body mass index; SD — standard deviation

MATERIAL AND METHODS

Sixty-nine (50K/19M) patients with rheumatic diseases who had completed at least one clinical trial were included in the study. The mean age of patients included in the study was 50.8 ± 12.9 years and the mean duration of disease was 13.1 ± 9.3 years. In the study group, 40 (32K/8M) patients had RA, 17 (8K/9M) patients had psoriatic arthritis (PsA), 7 (6K/1M) patients had systemic lupus erythematosus (SLE) and 5 (4K/1M) patients had other rheumatic diseases.

Baseline data on the patients included in the study are shown in Table 1.

Patients included in the study came from four different clinical trial centres located in Bydgoszcz (two centres), Torun and Warsaw, and signed an informed patient consent form to participate in the proposed study.

The study was conducted in 2021. The only criterion for inclusion in the study was the completion of at least one clinical trial before completing the questionnaire — a self-administered survey.

Height and weight were measured in each patient.

Each patient was asked to complete a questionnaire. The questionnaire was used for collecting demographic data, including subjective assessment of both financial status and health status before and after the clinical trial, reasons for enrolling in the clinical trial and hopes associated with it.

Patients were informed before completing the questionnaire that the survey was anonymous and were asked to answer each question as honestly as possible. Patients completed the questionnaires independently, in a comfortable environment and without time pressure.

The questionnaire was designed to collect demographic data on the patients, assessing their socioeconomic status, quality of life and emotions related to their participation in the clinical trial. The answers to the questionnaire were meant to be used for creating a description and identify characteristic features of patients participating in clinical trials.

STATISTICAL ANALYSIS

Results are presented as mean ± standard deviation (SD) for continuous variables. For categorical data, the results were presented as a numerical value and percentage.

For independent continuous data, an independent t-test was used when comparing two groups. A χ^2 test was used for comparison of categorical data. $P \leq 0.05$ was considered statistically significant.

MedCalc® Statistical Software version 20.120 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2022) was used for calculation and drawing of graphs.

RESULTS

Tables 2–5 show the basic data on the socioeconomic status of the patients included in the study.

Table 6 shows the subjective assessment of patients' health status before and after inclusion in the clinical trial.

DISCUSSION

When analysing the data presented in Tables 1–7, the profile of a patient participating in clinical trials forms a logical whole. It is important to note the conditions specific to Poland before attempting to describe the average patient who participates in and, most importantly, completes a clinical trial.

Access to biological therapies in Poland under the National Health Fund (NHF) is very low. The percentage of patients with rheumatic diseases who receive biological therapies is in the order of 2% [9]. This is partly related to the criteria a patient has to meet to start this type of treatment under the NHF. For example, in Drug Programme B.33, patients must

Table 2. Education level of patients included in the study

	Entire group (n = 69)
Incomplete primary [n]	0 (0%)
Primary [n]	4 (6%)
Vocational [n]	19 (27.5%)
Secondary [n]	27 (39%)
Higher [n]	19 (27.5%)

Source: authors' own study

Table 3. Subjective assessment of patients' financial status

Financial status	Number of patients [n]
Poor	4 (6%)
Average	41 (59%)
Good	23 (33%)
Very good	1 (1%)

Source: authors' own study

Table 4. Patient status

	Entire group (n = 69)
Patient lives with their family [n]	59 (86%)
Patient lives alone [n]	10 (14%)

Source: authors' own study

Table 5. Source of livelihood

	Entire group (n = 69)
Professional work [n]	42 (61%)
Invalid pension as a result of rheumatic disease [n]	9 (13%)
Early retirement pension as a result of rheumatic disease [n]	4 (6%)
Invalid pension/early retirement as a result of other diseases [n]	11 (16%)
Dependent on family [n]	3 (4%)

Source: authors' own study

Table 6. Subjective health status assessment

Health status assessment	Before trial [n]	After trial [n]	p
Excellent	0 (0%)	1 (1%)	< 0.0001
Very good	3 (4%)	15 (22%)	
Good	4 (6%)	47 (68%)	
Poor	39 (56%)	4 (9%)	
Very poor	23 (33%)	0 (0%)	

Source: authors' own study

have previously been treated for at least three months with a minimum of two disease-modifying drugs (DMARDs), and in both cases the therapy must have been ineffective and the patient must have high disease activity at the time of trial inclusion [9]. Under the terms of Drug Programme B.33, the disease activity score (DAS28) must be greater than 5.1 which, compared to most European countries with a required DAS 28 greater than 3.2, is a significant limitation in the availability of therapy. From a clinical point of view, the conditions for inclusion in such programmes are very restrictive, resulting in a low percentage of patients who are eligible for this type of treatment in Poland.

Unfortunately, it is not the case that disease progression in e.g., RA is only apparent when disease activity is high. Several large scientific studies indicate that also patients with low disease activity or even clinical remission may experience deterioration over the following months, including progression of radiological changes that are irreversible [10].

Table 7. Presence of comorbidities

	Entire group (n = 69)
At least one comorbidity [n]	41 (59%)
Degenerative disease [n]	12 (17%)
Diabetes [n]	10 (14%)
Hypertension [n]	26 (38%)
Other* [n]	17 (25%)

*Heart diseases, diseases of the digestive system, diseases of the urinary system, thyroid diseases, osteoporosis; Source: authors' own study

According to the current knowledge, even joint inflammation at a subclinical level — i.e., when the patient has no pain or swelling in the joint and only vascular flow is visible on power Doppler ultrasound or magnetic resonance imaging — may lead to an exacerbation of the disease within a few months [10].

For the above-mentioned reasons, conducting aggressive treatment according to the treat-to-target strategy is advisable in patients with moderate or low disease activity. This not only reduces the risk of disease progression but also provides patients with a better qua-

lity of life. Patients treated with biologics are much more economically and socially active, as their physical health and mental health improve thanks to this type of therapy.

Modern therapies, especially for chronic diseases, are associated with high costs when patients attempt to access treatment privately. Even in the current situation, where biosimilars are already on the market, the cost of this type of treatment can be considered high in the Polish reality.

Therefore, if patients do not meet the eligibility criteria for Drug Programmes, their treatment options are very limited. Hence, clinical trials may be an attractive alternative for them.

These are predominantly people with a secondary or higher education. As a result, they are able to filter information, which makes them see the benefits of participating in a clinical trial, and the clinical trial stories mentioned in the introduction do not discourage them in such a case.

The majority of patients enrolling in clinical trials rate their health status as poor or very poor. This may be considered not to be an entirely subjective assessment if the average disease duration, prevalence of comorbidities and high body mass index in the study group are taken into account. This means that, from a clinical point of view, these patients are also people on whom the underlying disease has already made its mark and they are looking for ways to improve or maintain their current health status.

An additional motivation to participate in clinical trials in this group of people is that most of them live with their families and are economically active. This gives them an incentive to take care of their health for both social and economic reasons.

CONCLUSIONS

Based on the analysis of the results obtained, the following conclusions were drawn about the patients participating in clinical trials:

1. These are people who have been ill for many years and who have also developed comorbidities, which further reduce their quality of life;
2. These are economically active people with an average financial situation, which in a way forces them to seek access to modern therapies by participating in clinical trials;
3. These are very often people with secondary or higher education.

ARTICLE INFORMATIONS AND DECLARATIONS

AUTHOR CONTRIBUTIONS

None.

FUNDING

None.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

None declared.

References

1. Waxman HA. The lessons of Vioxx--drug safety and sales. N Engl J Med. 2005; 352(25): 2576–2578, doi: 10.1056/NEJMp058136, indexed in Pubmed: 15972862.
2. Kim JH, Scialli AR. Thalidomide: the tragedy of birth defects and the effective treatment of disease. Toxicol Sci. 2011; 122(1): 1–6, doi: 10.1093/toxsci/kfr088, indexed in Pubmed: 21507989.
3. Hoffman J. New York City foster home accused of unethical AIDS drug trials. Nat Med. 2005; 11(1): 5, doi: 10.1038/nm0105-5b, indexed in Pubmed: 15635423.
4. Ahmad K. Ethics of AIDS drug trials on foster children questioned. Lancet Infect Dis. 2005; 5(6): 333–334, doi: 10.1016/s1473-3099(05)70128-6, indexed in Pubmed: 15948313.
5. Goldman DA. Thalidomide use: past history and current implications for practice. Oncol Nurs Forum. 2001; 28(3): 471–477, indexed in Pubmed: 11338756.
6. Krumholz HM, Ross JS, Presler AH, et al. What have we learnt from Vioxx? BMJ. 2007; 334(7585): 120–123, doi: 10.1136/bmj.39024.487720.68, indexed in Pubmed: 17235089.
7. Garner S, Fidan D, Frankish R, et al. Rofecoxib for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2002(2): CD003685, doi: 10.1002/14651858.CD003685, indexed in Pubmed: 12076502.
8. Anderson A, Borfitz D, Getz K. Global public attitudes about clinical research and patient experiences with clinical trials. JAMA Netw Open. 2018; 1(6): e182969, doi: 10.1001/jamanetworkopen.2018.2969, indexed in Pubmed: 30646218.
9. Obarska I. Nierówność w dostępie do leczenia biologicznego w chorobach autoimmunizacyjnych w Europie. Refundacja apteczna szansą na poprawę efektywności leczenia w Polsce. Polski Związek Pracodawców Przemysłu Farmaceutycznego, Warszawa 2022.
10. Terslev L, Ostergaard M. Rheumatoid arthritis relapse and remission — advancing our predictive capability using modern imaging. J Inflamm Res. 2021; 14: 2547–2555, doi: 10.2147/JIR.S284405, indexed in Pubmed: 34163211.