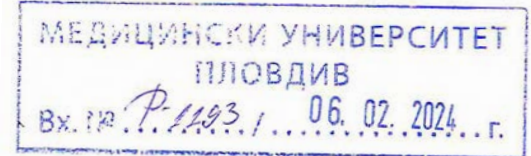




To the chairman of the scientific jury,
As determined by Order № P383/29.01.2024.
Issued by the Rector of Medical University – Plovdiv
15A, “Vasil Aprilov“ blvd.
4002 Plovdiv



REVIEW

By

Assoc. Prof. Antoaneta Toncheva, MD, PhD

On

Dissertation for the attainment of educational and scientific degree of “DOCTOR”

Field of higher education: 7. „Healthcare and sport“
Professional field: 7.1. „Medicine“
Doctoral program „Rheumatology“

”Compliance with and persistence of biologic treatment in patients with rheumatoid arthritis among Bulgarian population“

Author: Stefka Kamenova Neycheva, MD

Form of doctoral studies: independent preparation

Department: Propedeutics of internal diseases „Prof. Dr. Anton Mitov“

Scientific supervisor: Assoc. Prof Rosica Karalilova, MD, PhD, DSc

The provided set of materials on paper/electronic media is complete and in accordance with Article 70 (1) of Section I. Acquisition of the educational and scientific degree “Doctor” is in accordance with the Regulations of Medical university of Plovdiv (dated January 28, 2021), the Law on the Development of Academic Staff in the Republic of Bulgaria, its Rules and Regulations for application.

Brief biographical Information about the doctoral student:

Dr. Stefka Kamenova Neycheva was born on November 2, 1981, in Plovdiv. In 2000, she completed her secondary education at the Language High School in Plovdiv, and in 2006, she graduated in Medicine from the Medical University of Plovdiv. The doctoral student obtained a specialization in “Internal Medicine” in 2013, and in December 2016 – a specialization in “Rheumatology”. Since 2017, she has been working as a rheumatologist in the Rheumatology Department at Military Medical Academy-Sofia. From December 2022 to January 2024, Dr. Neycheva has been a free doctoral student in the Doctoral Program in Rheumatology at the department of Propedeutics of Internal Diseases. Prof. Dr. Anton Mitov, Faculty of Medicine, Medical University of Plovdiv.

1. Relevance of the Problem Examined in the Dissertation in Scientific and Scientific-Applied Aspect.

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease that not only affects the musculoskeletal system but also manifests with numerous extra-articular symptoms. Disability, reduced productivity at an early age, and premature mortality define its significant socio-economic impact. The development and introduction of biological disease-modifying antirheumatic drugs (bDMARDs) mark a true turning point in understanding the treatment, disease activity, and remission of the condition. Scientific studies and real-world practice have shown that these drugs halt structural damage, achieve low disease activity, and improve the patient's quality of life. Despite the positive therapeutic results reported in various clinical studies, adherence to the prescribed therapy in real-life situations remains low for several reasons. This underscores the need to evaluate the factors influencing patient compliance and persistence with the prescribed treatment. Enhancing patients' adherence to the biological therapy prescribed by rheumatologists largely determines the effectiveness of the treatment, disease activity, and the overall outcome of the disease.

The literature review is well-structured, informative, and sufficiently comprehensive. It is written with an adequate volume, demonstrating the dissertant's excellent awareness. A good analysis of the factors influencing the problem and their connection to the quality of life and functional status of the patient has been conducted.

The practical and scientific significance of the problem is indisputable. The study could help the rheumatologists attempt to influence modifiable factors, thereby improving adherence to the

prescribed biological treatments to achieve longer-lasting and better therapeutic results. This could contribute to building greater trust in the doctor-patient relationship, improving the quality of life and functional status of patients, and demonstrating that treatment with these medications brings more benefits than health risks.

The published data on this topic in the global literature are conflicting and challenging to compare due to different assessment methods and the variety of biological agents being compared. Few sources conduct analyses on adherence to such a large number of biological medications. To date, there has been no link established between factors influencing compliance/persistence to biological therapy in patients with rheumatoid arthritis and the functional status/quality of life in these patients with this inflammatory joint disease.

2. Knowledge of the Problem

Your presented dissertation is written in 139 standard printed pages, complemented with 15 figures and 90 tables. The candidate demonstrates a very good understanding of the problem. A detailed, in-depth, and balanced literature review has been conducted, showcasing a rich knowledge of the topic and the ability to select and critically analyze the necessary information. The bibliography includes a total of 158 sources, with 155 in Latin script and 3 in Cyrillic. The review is exhaustive, focusing on the goals and tasks of the dissertation without delving into irrelevant information. It concludes with arguments supporting the potential benefits of understanding the factors influencing patient adherence to prescribed treatment with biological disease-modifying antirheumatic drugs (bDMARDs).

3. Objectives, Tasks, and Methodology of the Problem.

The introduction is clearly formulated and reflects the directions of the addressed problem and the necessity for its development. The objectives are appropriately chosen, precisely and clearly formulated, and scientifically justified. Two objectives are formulated, with the first being scientific and the second practical. The tasks logically follow the set objectives. The number of participants is sufficient to fulfill the set tasks and achieve statistical significance in the results. The inclusion and exclusion criteria used for patient selection in the clinical study are correctly defined, taking into account the characteristics of the Bulgarian population and aligning with global recommendations for the treatment with biological disease-modifying antirheumatic drugs (bDMARDs).

The materials and methods are precisely selected and adequately directed towards each of the set tasks. The protocol for conducting the clinical trial is thoroughly described, along with the chronology of participation in the trial.

4. Results

The results for the tasks are clearly presented and well-illustrated by tables and figures. The methods used and the results of statistical analyses are thoroughly described. Tracking is conducted not only among the factors influencing adherence to different classes of biological medications but also establishes an important connection with the quality of life and functional status of the patients.

The discussion of the results logically compares the outcomes based on the author's own observations and research with those reported in the global literature. Contradictory results and the characteristics of the Bulgarian population of patients are the basis for writing the dissertation.

The conclusions are clearly formulated for each individual task and collectively for the overall theme of the study. Dr. Stefka Neycheva extensively and comprehensively investigates compliance and persistence toward different classes and subclasses of biological medications among the Bulgarian population of rheumatoid arthritis patients, examining the factors influencing adherence to prescribed treatment.

5. Evaluation of Publications Related to the Dissertation

In connection with the dissertation, three publications are presented - one in a foreign journal with an Impact Factor (IF) of 4.0 for the year 2022 and two in national journals. The number of scientific works meets the quantitative criteria outlined in the regulations of the Medical University - Plovdiv.

6. Personal Involvement of the Doctoral Candidate

The doctoral candidate actively participated in conducting the studies related to the dissertation, their synthesis, and analysis. In all articles and communications, Dr. Neycheva is the first author, which supports the assertion that the dissertation work is her personal contribution.

7. Abstract

The abstract contains 54 pages and serves as a summary of the dissertation. It provides an opportunity for a visual and comprehensive understanding of the objectives, tasks, results, discussion, conclusions, and contributions of the work. It reflects the main results achieved in the dissertation and is well-illustrated with tables and graphs.

8. Critical notes and recommendations

I have no critical remarks or recommendations for the dissertation work. The work has a fully completed form, and the set goals and tasks have been achieved. The conclusions are logical and valuable.

9. Conclusion

The presented dissertation on the topic "Compliance with and Persistence of Biological Therapy in Patients with Rheumatoid Arthritis in the Bulgarian Population" is a timely and in-depth comprehensive study with clearly formulated objectives, tasks, and results, contributing significantly

to contemporary rheumatology. The dissertation addresses an unexplored topic in Bulgaria, and the obtained results have scientific and practical contributions to rheumatology both locally and internationally. The dissertation fully complies with the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of law, and the relevant Regulations of Medical University - Plovdiv. The doctoral candidate demonstrates in-depth theoretical knowledge and professional skills. Based on the above, I provide my positive evaluation for the award of the educational and scientific degree of "Doctor" to Dr. Stefka Kamenova Neycheva in the field of higher education: 7. Healthcare and sports, professional direction: 7.1. Scientific specialty "Rheumatology."

Date: 01.02.2024 г.

Reviewers: Assoc. prof. Antoaneta Toncheva, MD, PhD

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Заличено на основание
Чл.5 §1, б."В" Регламент (ЕС)2016/679