



## STATEMENT

By

**Prof. Anastas Batalov, 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“

**Faculty of Medicine, MU-Plovdiv**

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

## **1. Presentation of the procedure and the PhD candidate**

The statement is prepared in an accordance with an Order No: P-383/29.01.2024 of the Rector of MU-Plovdiv, Prof. Angel Uchikov, MD, PhD, DMSc. Dr. Neycheva submitted all the required materials and documents for the purposes of the competition within the deadline, both in hard copy and electronic format, in accordance with Article 70 (1) of Section I of the Regulation for Academic Development of MU-Plovdiv dated January 28, 2021. These include: European format autobiography, dissertation work in hard copy and electronic format, abstract in Bulgarian in hard copy and electronic format, abstract in English in electronic format, a list of publications on the topic (3 in total), copies of the publications, notarized diploma for the educational qualification of "Master," order of enrollment in the doctoral program, protocol from the Doctoral School for dismissal with the right to defense, protocol from the doctoral minimum exam, declarations of originality and authenticity of the attached documents, and a certificate for the obtained credits from the group study plan.

## **2. Relevance of the Topic**

Rheumatoid arthritis (RA) is a chronic, disabling, inflammatory joint disease associated with progressive joint damage and impaired quality of life without appropriate and timely treatment. The discovery and introduction of the biologic drugs targeting specific pro-inflammatory molecules have allowed the introduction of terms such as "remission" and "low disease activity," enabling the development of the "treat to target" strategy. Despite the good therapeutic results reported by dozens of randomized clinical trials, adherence to the therapy for this systemic inflammatory disease remains unreasonably low, often below 20%. The factors influencing adherence to the prescribed therapeutic plan can be divided into three groups: 1) Individual patient characteristics and health status; 2) Disease characteristics; and 3) Therapeutic effectiveness. Understanding modifiable and non-modifiable factors can assist rheumatologists in selecting a medication, influencing the patient understanding of their disease, thereby improving the treatment adherence and the doctor-patient relationship.

The presented dissertation addresses an issue of significant health and socio-economic value. The data published on this topic in the global literature are contradictory. Individual authors conduct analyses on the compliance and persistence towards such a large number of biological medications. For the first time, a link has been sought between factors influencing adherence to prescribed treatment, such as age, gender, disease duration, combination therapy with methotrexate, previous exposure to a biological agent, and functional capacity, disease activity, and quality of life.

## **3. Understanding the Issue**

The literature review is presented in 25 pages, with all 158 sources systematically and comprehensively compared and analyzed. The analysis is specific, devoid of unnecessary information, and analytically introduces the essence of the problem. Definitions are provided for all terms discussed in the

research. A thorough survey of the factors influencing the problem and their relationship with disease activity, quality of life, and functional status of the patient has been conducted.

#### **4. Characterization and Evaluation of the Dissertation Work and Contributions.**

The dissertation work is a comprehensive study dedicated to issues related to compliance and persistence towards treatment with biological agents in patients with rheumatoid arthritis (RA). The defined tasks are specific, aligned with the set objectives, and are sufficient for their accomplishment.

The study holds significant scientific and practical value. Understanding the factors affecting patient adherence to prescribed therapy will improve the doctor-patient relationship, enhance the therapeutic effectiveness of medications, improve the prognosis of rheumatoid arthritis, and reduce the state's expenses for treating complications arising from this debilitating disease.

#### **5. Materials and Methods**

In the "Materials and Methods" section, the research methods are described, outlining how the set objectives are addressed, and the criteria for determining the observation units. The protocol for conducting the clinical trial is detailed, along with the chronology of participation in the trial. The study was conducted retrospectively, with patients recruited from October 2014 to May 2017, and a follow-up period of 3 years (36 months) until December 2020.

#### **6. Description and Assessment of the Dissertation Work.**

**The presentation of the results** from the original research is thorough and well-illustrated with an adequate number of tables and figures. The work is correctly structured, containing all commonly accepted sections and parts. The methods used are described in detail, along with the results of statistical analyses. The large amount of data is well thought out and systematically organized.

**In the discussion**, the doctoral candidate demonstrates a strong understanding of the researched problem and an excellent ability to compare and interpret the results based on her own observations and research in comparison to those reported in the global literature.

**The conclusions** are clearly formulated, both for each individual task and overall for the studied theme of the work. Dr. Stefka Neicheva thoroughly and comprehensively investigates compliance and persistence toward various classes and subclasses of biological drugs among the Bulgarian population of rheumatoid arthritis (RA) patients, examining the factors that could influence adherence to prescribed treatment.

#### **7. Contributions and importance of the dissertation**

The dissertation provides valuable information regarding the factors influencing the adherence to the biological therapy among the patients with rheumatoid arthritis (RA). It also discusses the specific challenges

faced by both the physician and the patient. This has a significant scientific and practical value in the field of the rheumatology and health care more broadly.

## **8. Publications**

Three publications are presented in relation to the dissertation - one in a foreign journal with an impact factor of 4.0 in 2022 and two in national journals. The number of scientific papers meets the quantitative criteria outlined in the regulations of MU - Plovdiv.

## **9. Abstract**

The abstract consists of 54 pages and serves as a summary of the doctoral thesis. 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. It is well-illustrated with tables and graphs.

## **10. Critical notes or recommendations**

I have no critical comments or recommendations for the doctoral thesis. The work is thoroughly completed, the set goals and tasks are accomplished. The conclusions are logical and valuable

## **CONCLUSION**

The doctoral thesis contains scientific and applied results that constitute an original contribution to science, meeting all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of the Law, and the corresponding Regulations of MU - Plovdiv. The presented materials and dissertation results fully comply with the specific requirements of MU – Plovdiv.

The doctoral thesis demonstrates that the doctoral candidate, Dr. Stefka Kamenova Neicheva, possesses in-depth theoretical knowledge and professional skills in the scientific specialty of rheumatology, showcasing qualities and skills for independent scientific research.

Based on the above, I confidently provide my positive evaluation for the conducted research, presented in the reviewed doctoral thesis, abstract, achieved results, and contributions. I recommend to the esteemed academic jury to award/not award the educational and scientific degree of 'Doctor' to Dr. Stefka Kamenova Neicheva in the doctoral program in Rheumatology.

01. 02. 2024.

**Reviewer:** Prof. Anastas Batalov, DM, PhD

Заличено на основание  
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