

## REVIEW

From: Prof. Valentina Boyanova Petkova-Dimitrova Ph.D., Vice-Rector for Science and Accreditation, Medical University - Sofia, member of the scientific jury, included by Order № RD-38-628 / 22.12.2021 of the Rector of Sofia University "St. Kliment Ohridski ”.

Subject: procedure for the defense of a dissertation on the topic: "Health-related quality of life in patients with vasculitis associated with antineutrophil cytoplasmic antibodies conducting biological treatment" in the field of higher education - 7. Health and Sports Professional field - 7.3 Pharmacy Scientific specialty "Social Medicine and Organization of Health and Pharmacy" of pharmacist Tsvetomir Mario Deliiski, research supervisors: Assoc. Prof. Dr. Emil Hristov, Ph.D. and Assoc. Prof. Dr. Lyubomir Marinchev, Ph.D.

Assistant Mario Deliiski was born in 1973. He is a graduate of 142 Primary School with early foreign language training "Veselin Hanchev" - Sofia. In 2015 he successfully graduated from the Faculty of Pharmacy of the Medical University - Sofia and obtained a master's degree in Pharmacy. His career began as a consultant in a pharmacy, passed through the BDA where the candidate held the following positions - chief expert and head of department of various units. Since 2016 after a competition he was appointed an assistant at the Faculty of Chemistry and Pharmacy of Sofia University "St. Kliment Ohridski ”, where he still works.

The dissertation provided to me covers 145 pages and is structured as follows: Introduction - 7 pages, Literary review - 25 pages, Goals and objectives - 1 page, Materials and methods - 8 pages, Results of own research and analysis - 53 pages,

Discussion of the results - 3 pages, Main conclusions from the dissertation - 2 pages, References - 39 pages, Appendices. The structure of the dissertation, as well as the presented set of materials on electronic media is in accordance with the Regulations on the terms and conditions for obtaining scientific degrees and holding academic positions at Sofia University and includes the following documents: Enrollment order, expulsion order, resume, diploma for higher education, dissertation, abstract, certificate of passed exams, declaration of authorship, reference for doctor, plagiarism report, protocol for originality of the dissertation, statement of originality, instructions for verification of originality, order for scientific jury. All required documents are neatly arranged and in accordance with the requirements.

The topic developed in the dissertation concerns a group of rare diseases - systemic vasculitis, which affects different organs and systems with different degrees of severity depending on the size, location and importance of the affected vessels. The variety of these obscurations requires a multidisciplinary approach. The quality of life in standard vasculitis treatment does not meet modern requirements, therefore the use of biological drugs for the treatment of vasculitis is a therapeutic novelty and is of considerable clinical interest. Their use is expected to significantly improve health-related quality of life in patients diagnosed with vasculitis associated with antineutrophil cytoplasmic antibodies. This is proof of the relevance of the problem on which the dissertation's research is focused.

The overview part, as structured, traces the essence of this rare disease, acquainting us with the health problem, possible complications, assessment of disabilities, therapeutic approaches. The review provides a detailed analysis of research on the topic published so far, which in itself is a theoretical contribution to the field.

The summary of the review also shows the choice of further studies in the dissertation, namely the lack of health quality of life studies (HRQoL) in patients

with ANCA-associated systemic vasculitis treated with Rituximab. The integrity and completion of the review outlines the focus of further research.

A goal and six main tasks have been formulated, which have been successfully carried out in the course of the research.

The tools used include a two-center, prospective, observational, non-interventional, controlled study in two periods. The main method is to conduct a "direct individual survey", with closed answers by filling in the SF-36 version 2 questionnaire and the EuroQol 5D questionnaire in electronic format. Through the variety of methods used, which are skillfully combined to achieve the goal, the main task of a dissertation is achieved - to show that the dissertation master and apply in practice certain methodological knowledge.

The obtained results are demonstrated in six main parts - representativeness of the sample and demographic characteristics of the analyzed cohort; clinical characteristics of the studied group of patients; assessment of health status using the EuroQol 5D-5L instrument before conducting biological treatment; assessment of health status with the EuroQol 5D-5L instrument after Rituximab biologics; Assessment of health status using the SF-36v2 Health Survey tool before conducting biological treatment; assessment of health status using the SF-36v2 Health Survey tool after biological treatment. The results of the individual studies are interesting as stand-alone studies, but in their sequence and completeness represent a comprehensive analysis of the risks and opportunities for biological treatment.

The formulated conclusions correspond to the set tasks, so that the doctoral student has fulfilled his set goals and tasks. The developed dissertation thesis outlines the conclusion that conducting only conventional treatment does not lead to changes in the physical functioning, emotional state and sense of general health of patients.

Biological treatment leads to qualitative and quantitative improvement of all components of physical health - according to all indicators, patients are within the norms of the population.

The results of the dissertation are published in five scientific articles.

Contributions that can be differentiated can be grouped as:

- Scientific and theoretical contributions:

1. For the first time in Bulgaria a systematic study of patients with vasculitis associated with antineutrophil cytoplasmic antibodies conducting biological treatment is conducted.

2. For the first time in Bulgaria a retrospective analysis of the evolution of the disease in patients with vasculitis associated with antineutrophil cytoplasmic antibodies is performed by stratification and evaluation of clinical activity measured by the vasculitis activity scale BVAS-Persistent points.

3. For the first time in Bulgaria, health-related quality of life is measured in patients with vasculitis associated with antineutrophil cytoplasmic antibodies, before and after biological treatment using common instruments.

- Contributions of scientific and applied nature

1. An original protocol and design of a non-interventional, observational, prospective / retrospective study to measure health-related quality of life in the Bulgarian population of vasculitis patients associated with antineutrophil cytoplasmic antibodies before and after biological treatment has been developed.

2. Measurement of health-related quality of life in patients with AAB can be used for routine analysis of health before and after treatment.

- Contributory contributions:

1. Improving the health-related quality of life of patients with AAB provides additional arguments to justify biological treatment as an alternative, despite the relatively high cost of drug therapy.

According to the scientometric report for fulfillment of the minimum national requirements, the applicant exceeds the required points.

In conclusion, the dissertation on "Health-related quality of life in patients with vasculitis associated with antineutrophil cytoplasmic antibodies conducting biological treatment" by assistant Tsvetomir Deliiski, developed with the right goals and objectives, using adequate methodological tools and a reliable interpretation in the discussion of the results covers the requirements for obtaining the educational and scientific degree "Doctor". The proposed draft abstract fully reflects the essence of the work.

I accept that the work is an independent work of the dissertation and I suggest to the honored members of the scientific jury to give their positive vote and to award a mag.pharm. Tsvetomir Mario Deliiski educational and scientific degree "Doctor".

16.02.2022

Sofia

Reviewer:

/ Prof. V. Petkova, DSc/