

STATEMENT

From

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Regarding the dissertation of Dr. Asiyana Hristoforova Petrova entitled "Complex evaluation of the effectiveness of biological therapy in patients with active ulcerative colitis" for the degree "Doctor" in the professional field 7.1. Medicine, scientific specialty "Gastroenterology" code 03.01.14.

As a reviewer, appointed by Order № P-109-385/25.08.2023 of the Rector of the Medical University - Varna Prof. Dr. Svetoslav Georgiev, PhD and based on the Law on the Development of Academic Faculty in the Republic of Bulgaria I share the following opinion.

The subject of the dissertation of Dr. Asiyana Petrova is an important and topical problem for medical science and gastroenterology, related to patients with inflammatory bowel diseases. Their widespread occurrence and the increasing frequency of newly diagnosed patients represent a serious epidemiological and social problem. On the other hand, the young age of onset and the serious health and psychological problems it subsequently causes are a serious challenge for any gastroenterologist. In recent years, biological therapy has established itself as a method of treatment for these patients with a very good response effect. Dr. Petrova's dissertation work is focused on the clinical evaluation of the efficacy and safety profile of biological therapy in patients with active ulcerative colitis. In this regard, Dr Petrova's research is of great importance and current relevance.

The dissertation is presented in 180 pages, distributed as follows: Table of Contents - 7 pages, Introduction - 2 pages, Literature Review - 43 pages, Aim and

Objectives - 2 pages, Material and Methods - 6 pages, Results - 64 pages, Conclusion - 1 page, Algorithm - 1 page, Conclusions and Contributions - 2 pages, Bibliography - 21 pages, Attachments - 26 pages.

The proportion between the different sections is kept.

Introduction presents in a synthesized form the current view of inflammatory bowel diseases. It described the five elements necessary for treatment success.

The literature review is contemporary and begins with a discussion of the epidemiology and pathogenesis of inflammatory bowel disease. This is followed by a presentation of the natural evolution of these diseases, their extraintestinal manifestations, clinical indices to assess their activity and histological changes, with an important focus on mucosal healing. The various diagnostic methods - serum, faecal and imaging techniques are reviewed, with attention to non-invasive biomarkers. The imaging findings on colonoscopy of active ulcerative colitis are not described. The treatment of inflammatory bowel disease, both medical and surgical, is presented. The available drugs used as biological therapy are presented in detail. The reasons for lack of or loss of response to biological therapy, their drug monitoring and possible adverse side effects are described. The problems associated with impaired quality of life in these patients are then presented. There is a defended dissertation on quality of life in patients with inflammatory bowel disease and validation of a questionnaire that is not cited in this paper.

Impressive is the fact that such a complex matter is presented in a very elegant and understandable way, which shows that the author knows the subject in depth.

The aim and seven objectives are well formulated and are in direct consequence of the literature review presented.

The study cohort included 107 individuals with active ulcerative colitis - 55 men and 52 women, followed for the period 2015 to 2023. Inclusion and exclusion criteria are presented. The history, physical examination, laboratory data, instrumental and histomorphological investigations applied to the patients are presented in detail. A questionnaire method was used in 85 patients to assess quality of life and degree of fatigue. Modern methods of statistical data processing were used.

The results are well structured and illustrated, and the entire dissertation contains 32 figures and 71 tables. They are presented in several sections, according to the set tasks. I consider particularly important the results of section 5.10, which provides a comparative analysis of CRP, faecal calprotectin and total Mayo scoring for each biologic administered in this study. The elaborate lean tracking system for these patients included in a precise surveillance registry is noteworthy.

In response to the sixth task, an algorithm was developed to select the correct patient for the appropriate biological treatment regimen and predictors of treatment response. Of no less importance, in my opinion, is that a proposal for a biologic treatment algorithm for patients with active ulcerative colitis unresponsive to conventional therapy has been developed.

There is no classical concluding discussion after the presented results, as it is done at the end of each chapter, which I consider as a strength of the dissertation. This way of presenting the research contingent shows that the author has gone into depth on the chosen problem, and that he has good clinical thinking and professional training.

The nine conclusions drawn are specific, correct and in logical consequence of the results obtained. They reflect the obtained data in a completely accurate and generalized way. I would recommend that an elastographic image of the intestinal wall be applied to conclusion 5 in the future.

There are nine contributions of an applied and confirmatory nature, and I accept them in full. With particular importance I accept conclusions No 8 and No 9, as they are essential for improving the clinical follow-up of patients with inflammatory bowel diseases, which is still a problem in our country.

The publications and scientific communications related to the dissertation are five in total - quite sufficient according to the requirements. In all publications Dr. Petrova is the first author.

The bibliography cites 229 sources - 17 in Cyrillic and 212 in Latin. More than 2/3 of them are from the last 10 years. All authors cited are directly relevant to the problem under study and are cited correctly, where appropriate, according to the aim and objectives of the thesis.

In conclusion, based on the above, I believe that the dissertation work of Dr. Asiyana Hristoforova Petrova entitled "Complex evaluation of the effectiveness of biological therapy in patients with active ulcerative colitis" fully meets the requirements for the award of the educational and scientific degree "Doctor".

18.10.2023

Member of the Scientific Jury:

/Prof. Vladimir Andonov/

