

Option

From

Assoc.Prof.Dr. Lili Slavcheva Trifonova-Grudeva

MU-Varna, Faculty of Public Health, Board of Hygiene and Epidemiology, University Hospital "St. Marina"-EAD Varna - dietician

According to the Order № P-109-385/25.08.2023 of the Rector of Medical University-Varna I am elected as a member of the Scientific Jury in the procedure for the acquisition of the educational and scientific degree "Doctor" of Dr. Asiyana Hristoforova Petrova - PhD student in the independent form of study in the doctoral program "Gastroenterology", professional field 7.1.Medicine, enrolled by Order № P-109-124/27.03.2019, "Complex evaluation of the effectiveness of biological therapy in patients with active ulcerative colitis", with scientific supervisor Assoc.

On the basis of Protocol №1/07.09.2023, at the first meeting of the Scientific Jury I was appointed. The set of materials provided to me on paper and electronic media has been properly prepared in accordance with the requirements of the Law of the Republic of Bulgaria, the Regulations for its application and the Regulations for the Development of the Academic Staff of MU-Varna.

Brief biographical data

Dr. Asiyana Hristoforova Petrova was born in Gabrovo on 17.02.1988. She graduated from Natural Mathematics High School in the town of. She graduated from the University of Science and Technology in Gabrovo with a degree in Biology with full honors. She graduated in medicine at the Medical University in Gabrovo. In 2013 she graduated from Medical University in Varna with excellent grades. Dr. Petrova has been working at the Clinic of Gastroenterology since 2016, and since 2019 has been an assistant professor of gastroenterology at the Second Department of Internal Medicine of Medical University Varna. She obtained her specialty in Gastroenterology in 2021. He holds certificates of professional qualification in abdominal ultrasonography, upper and lower endoscopy - first and second level. He is fluent in English and has very good computer literacy. He is a member of the BMA and the Bulgarian Society of Gastroenterology, Gastrointestinal Endoscopy and Abdominal Ultrasonography.

The clinical study was conducted after obtaining permission from the research ethics committee at MU-Varna. All participants signed informed consent. intended to prepare an opinion.

Scientific significance of the chosen topic and innovativeness

The dissertation is devoted to an extremely important topic in modern medicine. Inflammatory bowel diseases have become a global worldwide problem in the last 50 years. Epidemiological studies indicate that their prevalence will affect nearly 30 million people by 2025. Ulcerative colitis, as an idiopathic bowel disease, can involve all compartments of the colon. Genetic factors, environmental influences, autoimmunity and the gut microbiome are major

contributors. The disease occurs in relatively young people and requires long-term and continuous drug therapy. The choice of treatment is determined by the course, extent, severity of the disease, often the lack of response and last but not least the safety of the treatment. The therapeutic goals for IBD and ulcerative colitis in particular have changed with the introduction of biologic therapy. These drugs have shown unequivocally that it is possible to control mucosal inflammation. It is equally important to determine the clinical severity of the disease in order to plan optimal therapy. Achieving durable remission is a major goal and challenge that is answered and solved in modern biological treatment. This makes the present work sufficiently relevant and dissertationable.

Characteristics and evaluation of the thesis

The dissertation consists of 180 pages and is illustrated with 32 figures and 71 tables. The literature cited includes 229 sources, of which 17 in Cyrillic and 212 in Latin. The appendices are 11 and represent 26 pages.

Discussed and referred for public defense by the Departmental Council of the Second Department of Internal Medicine of the Medical University, Brno. The first part of the study was presented at the Second Faculty of Internal Medicine, Varna.

The literature review is exhaustive and complete. It is entirely focused on the topic. It covers all aspects of the problem and logically brings out the rationale for conducting this clinical work. An in-depth analysis of a number of studies on the topic has been carried out. It shows extremely good scientific preparation and excellent awareness of the PhD student on the scientific problem as well as her ability to analyze and summarize the literature data.

The aim of the dissertation is clearly formulated: to perform a clinical evaluation of the efficacy and safety profile of the biological therapy in patients with active ulcerative colitis. The seven tasks are logically derived and correspond to the achievement of the stated goal.

Material and Methods. The study included 107 patients with active UC followed up in the Gastroenterology Clinic for the period 2015-01.08.2023. A retrospective analysis of medical records was performed in all subjects. The selected patients met well-defined inclusion and exclusion criteria. All patients underwent clinical examination, conventional laboratory tests, and non-invasive markers of inflammation, fecal calprotectin and CPP. Igra T-SPOT.TB/ QuantiFeron Test was performed in all patients to detect blood cells (T effector lymphocytes) responding to stimulation with Mycobacterium tuberculosis antigens. The test is based on the ELISPOT method, significantly more reliable than conventional ELISA methods.

Immunological tests - autoantibodies - p-ANCA, c-ANCA and ANA by indirect immunofluorescence and Westernblot (immunoblot) were performed in 5 subjects due to persistently elevated values of cholestatic enzymes to exclude/confirm primary sclerosing cholangitis.

To exclude the presence of superimposed bacterial infection, all patients were tested for Salmonella, Shigella, Escherichia coli, and Clostridium difficile before initiation of biologic therapy.

Therapeutic drug monitoring to detect the presence of anti-drug antibodies and the concentration of the biological agent in the blood by ELISA was analyzed in 17 patients. Abdominal ultrasonography was performed in all 107 patients, with examination of colonic wall thickness in mm, presence/loss of haustration, normal/absent peristalsis.

Comprehensive fibrocolonoscopy was performed before initiation of biologic treatment and every 12 months after initiation. Mayo subscore endoscopy was used to analyze the severity of UC. Quality of life and degree of fatigue were assessed in 85 patients with active UC.

Adequate, reliable statistical methods were used to ensure the reliability of the results and conclusions.

The detailed and detailed analysis of the results obtained and the comparison with data from numerous literature sources shows an exceptionally good knowledge of the subject matter on the part of the dissertator, which once again proves her excellent knowledge and competence in the problem under study.

As a summary, the present observation reveals the expected high effectiveness of biologic drugs as well as their safety in the treatment of active ulcerative colitis. Therapeutic monitoring is finding increasing application as a potential strategy for treatment optimization.

The discussion is made according to the modern requirements for structuring a dissertation, separately for each task.

Dr. Petrova draws 9 conclusions, which are a logical conclusion of the set goal and objectives.

I accept the 9 contributions, of which 7 are scientifically applied and 2 are confirmatory. For the first time in Bulgaria a complex evaluation of patients with active ulcerative colitis on biological therapy has been made.

Abstract. The abstract of Dr. Asiyana Petrova is detailed, prepared according to the procedural requirements and fully corresponds to the main results and scientific contributions of the dissertation.

Assessment of publications and personal contribution of the PhD student

In connection with the dissertation, 2 full-text publications and 3 scientific communications have been submitted to international and national symposia and conferences, all of which Dr. Petrova is the first author, indicating her leading role in scientific developments and results obtained.

I have no critical remarks to the dissertation and strongly recommend Dr. Petrova to continue and expand her research in future research work.

Conclusion

The dissertation work of Dr. Asiyana Petrova, dedicated to the introduction of biologics, has revolutionized the treatment of patients with active form of ulcerative colitis. The work reflects the high professional (and the Regulations for the Development of the Academic Staff of MU-Varna for the Acquisition of Educational and Scientific Degree "Doctor"

I confidently give my positive evaluation and I take the liberty to recommend the esteemed members of the Scientific Jury to vote positively for the award of the degree of Doctor of Education and Science to Dr. Asiyana Hristoforova Petrova.



Date 17 Oct 2023

Assoc. Dr. Lili Slavcheva Trifonova-Grudeva, PhD