STATEMENT OF OPINION

By Assoc. Prof. Dr. Antonia Yordanova Atanasova, MD, PhD,DSc
Member of scientific jury from Medical University of Varna, habilitated in professional direction 7.1 Medicine, Medical University of Varna
on a dissertation entitled
" ANTIVIRAL THERAPY IN CHRONIC HEPATITIS B- DYNAMICS OF VIRAL MARKERS AND LONG-TERM RESULTS "

For awarding the educational and scientific degree "Doctor"
in the doctoral program "Gastroenterology"
field of higher education: 7. Healthcare and sports,
professional direction 7.1 Medicine
Author: Dr. Yoana Svetlozarova Stoyanova,
full-time doctoral student in the "Gastroenterology" doctoral program, Faculty of Medicine, MU-Varna

I. Procedure

By order No. R-109-83/21.03.2024 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna based on a report with entry No. 102-537/ 15.02.2024 by Associate Professor Dr. Mira Valentinova Siderova, PhD - Head of second department "Internal Medicine", with decision according to protocol No. 18/ 11.03.2024 of the Faculty Council and report with entry No. 103-1361/ 15.03.2024 by Prof. Dr. Yoto Yotov, PhD - Dean of the Faculty of "Medicine" at the Medical University of Varna, and on the basis of Art. 24, para. 6 and Art. 30, para. 3 , art. 68, para. 1 of the Regulations for the development of the academic staff at MU-Varna, on the basis of Art. 71, para. 1, para. 2 and para. 4 of the Regulations for the development of the academic staff at MU - Varna, I am appointed to prepare a statement of opinion on the

dissertation work of Dr. Yoana Svetlozarova Stoyanova with the topic: "Antiviral therapy in chronic hepatitis B - dynamics of viral markers and long-term results", for acquisition of the educational and scientific degree "Doctor" in the doctoral program "Gastroenterology" in the field of higher education: 7. Healthcare and sports, professional direction 7.1 Medicine.
My statement of opinion complies with the requirements for forming statements of opinions for the acquisition of the educational and scientific degree "Doctor".

II. Brief biographical data

Dr. Stoyanova was born on February 1, 1993 in the city of Varna. She graduated from First language high school in the city of Varna with excellent results, majoring in English and German. In she 2018 graduated from Medical University "Prof. Dr. Paraskev Stoyanov" with excellent results. From October 2018 until April 2022 she was a resident doctor in gastroenterology at the Internal Medicine Clinic of St. Marina, Varna. From October 2019 she is a full-time assistant at the Department of Clinical Medical Sciences. From April 2022 she works at the Gastroenterology Clinic of St. Marina, Varna. In December 2022 she acquired a specialty in gastroenterology. From January 2020 she is a full-time doctoral student at the Second Department of Internal Medicine with the topic "Antiviral therapy in chronic hepatitis B - dynamics of viral markers and long-term results" with scientific supervisor Assoc. Prof. Dr. Irina Ivanova, PhD.

III. Structure of the dissertation

The dissertation is written in 94 pages: introduction 1 page, literature review 36 pages, aim and objectives 1 page, patients and methods 10 pages, results and discussion 36 pages, conclusions 2 pages-13 in number, contributions 4 in number, one with original character, bibliography 176 literary sources, 4

Bulgarian authors stand out there, two published in Cyrillic, and the remaining 174 publications are in Latin. The work is illustrated with 47 figures and 15 tables. The study was approved by the Research Ethics Committee at MU-Varna. All patients signed an informed consent to participate in the study. In order to optimize the processing, the results of the observations and clinical indicators are systematized in tabular form, in Excel Microsoft.

IV. Relevance and significance of the dissertation work.

According to the latest data from the WHO, about 300 million live with chronic hepatitis B virus infection, which is one of the main risk factors for the onset of chronic liver disease, leading to complications like hepatocellular carcinoma (HCC). Mortality is nearly 1 million people per year. A small percentage of those infected worldwide receive antiviral treatment. Modern therapy with HBV replication inhibitors improves patient survival and prevents progression of chronic liver disease. Clearance of HBsAg occurs in about 1% per year of people with chronic HBV infection. Transaminase activity, liver synthetic parameters, and creatinine clearance are usually investigated in monitoring antiviral treatment; abdominal ultrasound is regularly performed for early detection of HCC. The recently introduced multiparametric ultrasound to assess histopathological concepts such as inflammatory activity, fibrosis and steatosis is proving to be particularly useful. Expectedly, undetectable viral load (HBV DNA) by a sensitive PCR test is achieved during treatment with nucleoside/nucleotide analogues. That is why there is a need to search for new markers to monitor the effect of antiviral drugs in relation to the life cycle of HBV, such as the synthesis of viral proteins (HBsAg, HB core- HB core-related antigens). The present dissertation is an attempt to answer some of these challenges in clinical work with patients with chronic HBV infection during antiviral treatment.

V. Essence of the dissertation work

The goal is properly defined and the tasks are well systematized and structured. The outputs are synchronized with the tasks and prove that the objective has been achieved.

As a summary of the results, Dr. Yoana Svetlozarova Stoyanova found that the application of nucleotide/nucleoside analogs in hepatitis B is highly effective in inhibiting HBV replication, providing an initial virological response in 63% and maintenance of viral suppression, respectively HBV DNA <10 IU/ml in 90.4% and undetectable HBV DNA in 84.5% of those treated. HBsAg negativity with appearance of anti HBs antibodies, i.e. functional cure was observed in 4.8% (n=4) patients during the course of therapy. HB core-related proteins are detected in the blood of patients with long-term antiviral therapy and suppression of viral replication; with 67% of the examined patients having a level between 3 and 4 log10 IU/ml; patients with clearance of HBsAg have a detectable level of HBcrAg. The dissertation concludes with four well-formulated contributions.

VI. Publications and scientific activity.

Dr. Yoana Stoyanova's dissertation work includes three publications: one full-text scientific publication related to the topic of the dissertation work in a national journal as first author, 2 printed abstracts - also as first author. Dr. Stoyanova has also participated in two national forums as first author.

The dissertation work of Dr. Yoana Svetlozarova Stoyanova fully meets in terms of structure and content the requirements for acquiring the scientific and educational degree "doctor"

All of the above mentioned gives me the reason to vote positively and to suggest to the members of the Scientific Jury at the Medical University "Prof. Dr. Paraskev Stoyanov"-Varna, to vote positively for awarding the educational

and scientific degree "Doctor" in the doctoral program "Gastroenterology" to Dr. Yoana Svetlozarova Stoyanova.

24.04.2024 Statement of opinion prepared by:

Varna Assoc. Prof. Dr. Antonia Yordanova Atanasova, MD, PhD, DSc