

STATEMENT

by Prof. Hristo Tzekov, MD, PhD, DsC

On the dissertation of Dr. Maria Penkova-Ivanova "Expression of tumor reversion markers in colorectal cancer". Scientific supervisor of the dissertation is Assoc. Prof. Eleonora Georgieva Dimitrova-Gospodinova, MD, PhD.

The dissertation work of Dr. Maria Penkova-Ivanova is dedicated to a topical and key problem in patients with histologically verified colorectal cancer (CRC), namely the discovery and introduction of new prognostic biomarkers in the above group of patients.

Significant advances have been made in the diagnosis and treatment of CRC in recent decades, yet 5-year survival rates for patients with metastatic CRC remain low (less than 14%). In recent years, increasing attention has been paid to various biomarkers that may serve as new methods for screening, diagnosis, prediction and monitoring of response to treatment. There are a small number of publications in the literature investigating the potential association between TSTR expression levels and overall survival in different types of malignant solid tumors. Considering the difficulties and limitations in the treatment of this cohort of patients, the topic of Dr. Maria Penkova is relevant and has a significant contribution regarding the prognosis of patients with CRC.

The dissertation is written in 117 pages and contains the following sections: introduction - 2 pages, literature review - 58 pages, aim and objectives - 1 page, patient population and specific study methods - 11 pages, results - 12 pages, discussion - 4 pages, conclusion - 1 page, contributions - 1 page, scientific publications and communications related to the dissertation - 2 p. The reference list includes 274 authors and is presented on 19 p. The structure of the dissertation is well balanced, the proportions of the individual sections are

respected and meets the requirements of the Law for the Development of Scientific Staff in the Republic of Bulgaria.

A table of contents and abbreviations used are provided at the beginning of the thesis, which improves the graphical appearance and ease of understanding the thesis.

The introduction is clear and contains the main points of the individual chapters of the thesis. The literature review thoroughly and accurately describes the structure of TCTP, its biological function in cells, its role in the early stages of carcinogenesis, tumor progression and tumor reversion. Studies worldwide reflecting the relationship between TCTP expression levels and overall survival in carcinomas of different localization are summarized and illustrated by tables.

The aim is precisely formulated and corresponds to the topic of the thesis. The set tasks are in line with the stated aim.

The materials and the specific methods of the study are properly and accurately selected to fulfill the stated aim and objectives. Descriptive statistics, statistical clustering and data evaluation methods, nonparametric analysis, ROC analysis and survival analysis were used for statistical processing of the collected data.

In the chapter "Results" Dr. Penkova presents her own data from a study on 74 patients. The description of the results meets the objectives and is illustrated precisely with a large number of graphs, figures and tables.

The chapter "Discussion" shows the dissertation's ability to describe, analyze and summarize its own results. The studies and analyses performed show that there are significant differences in the survival of CRC patients depending on the expression levels of TCTP in the nuclei of the primary tumor cells. Analysis of the results showed that in the patient population studied, mean PFS and OS were significantly lower in the subgroup with higher nuclear expression of TCTP. Therefore, high nuclear TCTP expression levels are an independent prognostic factor for worse progression-free survival and overall survival.

The conclusions are 7 in total and reflect the results obtained. They are concise, clear and well summarized.

The abstract is 52 pages and contains the main chapters of the thesis.

In connection with the dissertation work 5 publications have been made, 3 of which are in international journals with impact factor . From the made reference it is established that the scientific activity of Dr. Maria Penkova fully meets the criteria for the defense of the educational and scientific degree "Doctor" of Medical University - Varna.

The topic of the dissertation is original, the results are significant, the contributions are substantial and the dissertation should receive a positive evaluation. The thesis of Dr. Maria Penkova meets the requirements of the Law on the Development of Academic Staff for the Acquisition of the Education and Science Degree „Doctor“. I propose the Honourable Scientific Jury to vote positively for the award of the PhD degree to Dr. Maria Penkova.

Drafted the opinion:

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

/Prof. Hristo Tzekov, MD, PhD, DsC/