

# STATEMENT

**from Assoc. Prof. Dr. Nikolay Vladimirov Conev, Ph.D.**

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According to order № P-109-110 / 11.03.2022 of the Rector of the Medical University - Varna and Protocol №1 / 25.03.2022, I was chosen to prepare a statement on the dissertation of Dr. Margarita Krasenova Maneva.

**On the dissertation thesis of Dr. Margarita Krasenova Maneva entitled "Predictive and prognostic value of a marker for necroptosis - RIPK3 in patients with colon cancer in metastatic stage" for the award of educational and scientific degree "Doctor" in "Oncology" , in the field of higher education "Health and Sports", professional field 7.1. "Medicine". The scientific supervisor of the dissertation is Assoc. Prof. Eleonora Georgieva Dimitrova - Gospodinova, Ph.D.**

The statement was prepared in accordance with the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria, the regulations for the development of the academic staff of MU-Varna and the specific requirements for obtaining the scientific degree "Doctor".

## **1. Biographical data of Dr. Margarita Krasenova Maneva**

- in 2015 graduated from the Medical University - Varna with a degree in Medicine;
- in the period January 2016 - November 2016 works as a resident doctor in SBALOZ "Dr. Marko A. Markov" - Varna, Department of Medical Oncology and Palliative Care;
- from November 2016 started working at the Clinic of Medical Oncology of University Hospital "St. Marina" - Varna;
- from March 2017 is a full-time assistant at the Department of Propaedeutics of Internal Medicine at MU - Varna, English language training;
- from 2018 is a doctoral student full-time form of study at the same department;
- is a member of the European Society of Medical Oncology (ESMO).

## **2. Assessment of the relevance of the topic, goals and objectives:**

According to the World Health Organization (WHO), colorectal cancer (CRC) is the third most common solid tumor worldwide, with a five-year survival rate in metastatic patients remaining low at only 8-10%. Necroptosis is a necrotic form of programmed cell death that plays a key role in regulating not only various normal physiological processes but also many diseases, such as inflammatory processes, ischemic damage, neurodegenerative diseases and malignancies. The dissertation of Dr. Margarita Krasenova Maneva considers a current topic about the role of one of the essential markers of necroptosis - RIPK3 as a prognostic and predictive factor in patients with CRC in the metastatic stage.

## **3. Structure of the dissertation:**

The dissertation is well structured and contains the following main parts:

- Introduction / 2 pages / - accurately and clearly identifies the main points on which the topic of the dissertation will be focused
- Literary review / 57 pages /, which presents in-depth and expert knowledge on the topic of development
- Purpose and tasks / 1 page / - precisely formulated goal, which is a logical continuation of the literature review. The tasks, which are five in number, are specific and correspond to the question asked.
- Patient population and research methods / 10 pages / - well selected and thoroughly analyzed.
- Results / 11 pages / - the results of the retrospective study are presented in detail and well illustrated, which included 74 patients with metastatic CRC who underwent I line 5-FU based chemotherapy in the period January 2012. until December 2015
- Discussion / 4 pages / - the dissertation skillfully synthesizes and compares the results, showing good knowledge of the topic.
- Conclusions / 1 page / - briefly and accurately provide summary information about the work and its results, fully meeting the goals and objectives.
- Contributions / 1 page / - Dr. Maneva precisely points out the exceptional importance of the dissertation for Bulgaria and worldwide.
- Bibliography, including 227 Latin literature sources.

- Abstract / 44 pages / - well provided concise information on the main points marked in the dissertation.

#### **4. Literary awareness**

In her dissertation, Dr. Maneva provides a detailed and expert analysis of the topic. Attention is paid to the CRC, its epidemiology, tumorigenesis, signaling pathways, as well as the predictive and prognostic markers used. Impressive is the large database of information presented by the dissertation and his good knowledge in the field of necroptosis.

#### **5. Analysis of the conclusions and contributions**

Based on the obtained results, 5 conclusions were skillfully synthesized, which are clear and specific. The contributions formulated by Dr. Maneva prove the exceptional importance of the dissertation due to the fact that for the first time in Bulgaria the relationship between the level of expression of the marker for necroptosis RIPK3 in patients with mRCC is studied. The contribution of the work is even more important worldwide, as for the first time in the world literature the connection between the essential marker for necroptosis RIPK3 and the response to treatment with 5-FU based first-line HT in patients with mRCC is reported.

#### **6. Conclusion:**

The dissertation of the dissertation of Dr. Margarita Krasenova Maneva on "Predictive and prognostic value of a marker for necroptosis - RIPK3 in patients with colon cancer in metastatic stage" presents a current topic, whose results and conclusions are original contributions to science. The conclusions made are correct and well-founded. The development of the dissertation shows that the dissertation has in-depth theoretical knowledge in the scientific specialty of medical oncology. Having in mind the above, I give a positive assessment of the dissertation of Dr. Margarita Krasenova Maneva and recommend to the esteemed Scientific Jury to award her the scientific and educational degree "DOCTOR".

Date: 04.05.2025.  
Varna

Assoc. Prof. Dr. Nikolay Conev, Ph.D.

