

To: The Chairman of the Scientific Jury,
Appointed by Order No 109-131 from 20.02.2025
Of Prof. Dimtar Raykov, MD, PhD, D.Sc.,
Rector
Medical University
"Prof. Dr. P. Stoyanov"- Varna

STATEMENT

by Prof. Dr. Marianna Petrova Yaneva, MD, PhD, DSc

Title of the dissertation thesis:

"INVESTIGATING THE EXPRESSION OF NECROTIC CELL DEATH MARKERS AND
THEIR PREDICTIVE VALUE IN NEOADJUVANT CHEMORADIOTHERAPY OF
LOCALLY ADVANCED RECTAL CARCINOMA"

for dissertation thesis for the acquisition of the educational and scientific degree "PhD"

Ph.D. Candidate: Temenuzhka Rumenova Radeva- Petkova, MD

area of higher education 7. Healthcare and sports,
professional direction 7.1.

Medicine, scientific specialty "Medical radiology and Roentgenology speciality (including use of
radioactive isotopes)"

Ph.D tutor

Prof. Elitsa Petkova Encheva- Mitsova, MD, PhD

The presented PhD thesis comply with the regulations for obtaining a PhD degree, in accordance with the Law on the Development of the Academic Staff in the Republic of Bulgaria. Dr. Radeva's dissertation focuses on a current and highly relevant problem: identifying a reliable biomarker for predicting the response to neoadjuvant radiotherapy combined with chemotherapy (nCCRT).

Nine tasks have been set to prove this hypothesis. The concentrations of HMGB1 in the serum of patients with locally advanced rectal carcinoma (LARC), both before and after the treatment, are significant for the therapeutic outcomes. The study includes a total of 65 patients with LARC, all over 18 years of age. The data analysis is prospective. Histology has been confirmed for all patients. For 45 patients, the tumor was localized in the middle third of the rectum, while for 20 patients, it was in the lower third. The inclusion and exclusion criteria for the study have been defined. Patients were grouped based on gender, age, tumor differentiation, and the T and N stages. The imaging techniques used for staging before the start of treatment include: MRI, PET/CT, CT. The serum concentration of HMGB1 was determined using ELISA, before the start and at the end of the course of nCCRT. The stages of the treatment process are thoroughly detailed. Two fractionation regimens have been applied. In dosimetric planning, IMRT and VMAT irradiation techniques were used in combination with IGRT. Chemotherapy with Capecitabine was administered to all patients. The methods for assessing the tumor response rate.

- 1. Clinical: digital rectal examination; 2. Colonoscopy with biopsy; 3. Imaging methods; 4. Surgical intervention; 5. Histology

Four types of responses were reported: complete response, partial response, progression, and stable disease.

Statistical methods: Analysis was performed using the SPSS software package, version 19. The following analyses were conducted: descriptive analysis, non-parametric methods, correlation analysis, Kaplan-Meier survival test, regression analysis, and ROC analysis.

The treatment of rectal carcinoma includes a combination of radiotherapy and chemotherapy. Patient's response depends on their resistance to treatment. At this point, predictive

biomarkers are needed to assess their treatment response. The dissertation highlights predictors of therapeutic effectiveness, specifically the changes in serum concentration of HMGB1. High HMGB1 level and its dynamics serves as important marker of poor therapeutic response. This will indicate the need to explore alternative therapeutic options and a different approach to manage the disease. Higher HMGB1 expression is a negative prognostic factor associated with poorer overall survival.

In the literature review, 262 sources were analyzed, only two were in Bulgarian. The authors confirm the obtained results, indicating that this topic has not been extensively studied in Bulgaria, making the PhD candidate a pioneer in this field. Personalized treatment is a key focus in modern radiotherapy and chemotherapy. The dissertation presents eight conclusions and nine contributions.

Dr. Radeva graduated High School of Mathematics and completed her medical degree with excellent results. She speaks English.

In relation to the dissertation, three papers have been published. Dr. Radeva meets the criteria for the defense of the educational and scientific degree of "PhD." Her scientific activity fully satisfies the requirements for dissertation defense.

In the dissertation presented for defense, Dr. Radeva proves her ability to think scientifically, select and process scientific material, analyze data, formulate conclusions from the successful and challenging research conducted. Dr. Radeva is the first author in two of the publications. The dissertation meets all the requirements of the Law on the Development of Academic Staff and presents the PhD candidate as a experienced researcher in the field of identifying markers for assessing the treatment of rectal carcinoma.

Considering all mentioned above, I propose to the esteemed members of the scientific jury to vote positively for the acquisition of the educational scientific degree "PhD" by Temenuzhka Rumenova Radeva- Petkova, MD, in the scientific specialty "Medical Radiology and Roentgenology, including the use of radioactive isotopes".

31.03.2025

Prof. Dr. Marianna Petrova Yaneva. MD. PhD. DSc

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