

PEER REVIEW

IN REFERENCE TO:

Conducting a procedure for defense of the dissertation thesis of Temenuzhka Rumenova Radeva- Petkova, MD entitled:

"INVESTIGATING THE EXPRESSION OF NECROTIC CELL DEATH MARKERS AND THEIR PREDICTIVE VALUE IN NEOADJUVANT CHEMORADIOOTHERAPY OF LOCALLY ADVANCED RECTAL CARCINOMA" for obtaining the educational and scientific degree " PhD" in 7. Healthcare and Sports-higher education area, 7.1Medicine-professional field, Medical Radiology and Roentgenology speciality (including the use of radioactive isotopes).

I have been appointed as a member of the scientific jury and present peer review on the dissertation work by Order № R-109-131/20.02.25 of rector Prof. Dimitar Raykov, MD, PhD, Medical University –Varna.

The peer review is prepared by:

PROF.IGLIKA SPASOVA MIHAYLOVA, MD, PhD

Head of department of radiotherapy

The University SHAT of Oncology "Prof. Ivan Chernosemski"-EAD,Sofia

Dear members of the Scientific Jury,

Temenuzhka Rumenova Radeva- Petkova, MD, graduated from the Medical University of Varna Varna in 2013. From September 2013 to 2014 she worked at the University Hospital "St. Anna" in emergency pediatric department.

Since 2015 she started as physician at the Clinic of Radiotherapy, University Hospital "St. Marina," Varna, and from 2016 is an assistant professor at the Department of "Nuclear medicine, metabolic therapy and Radiotherapy," Medical University of Varna. She conducts classes for medical and dental students in Bulgarian and English.

In 2023, she acquired her Certificate of Completion of Special Training in "Radiotherapy". On April 24th 2017, she became a Ph.D. student in the self learning form in Medical Radiology and Roentgenology specialty (including the use of radioactive isotopes) at the Department of "Imaging Diagnostics, Interventional Radiology and Radiotherapy," Medical University, Varna. On 13.05.23 she was discharged with the right to defence.

Temenuzhka Rumenova Radeva-Petkova, MD speaks English and German.

She is a member of:

- European Society for Radiation Oncology (ESTRO)
- Guild of radiation oncologists in Bulgaria.

The scientific advisor of the dissertation is Prof. Elitsa Petkova Encheva, MD, PhD.

The dissertation thesis is written on 140 standard pages and includes 16 tables and 57 figures. It contains the following sections: Introduction- 2 pages, Literature Review- 47 pages, Aim and Tasks -1 pages, Materials and Methods- 13 pages, Results- 41 pages, Discussion- 7 pages, Conclusions- 1 pages, Contributions- 1 pages.

The dissertation thesis is well structured, the proportions of the separate sections are balanced and it meets the requirements of the Law for Development of the Academic Staff in the Republic of Bulgaria.

References include 262 literary sources, of which two are in Bulgarian and 260 are in English.

In the beginning of the dissertation, contents and used abbreviations are provided which makes the thesis easier to read.

The introduction is short and clear and contains the main aspects underlying the presentation of the individual chapters of the dissertation. The literature review thoroughly analyzes the sources revealing epidemiological, diagnostic, treatment, and prognostic factors in patients with rectal cancer. The unspecified and debatable problems related to predictive factors for response to neoadjuvant chemoradiotherapy of locally advanced rectal cancer are addressed in order to reduce early and late toxicity. The conclusions from the literature review lead to the essence of the present scientific work.

The aim is precisely formulated and corresponds to the topic of the dissertation. The tasks are 9 in number and are in accordance with the set aim.

The material and the methods are correctly and precisely selected to fulfill the set aim and tasks.

For the purpose of statistical data processing, the programming language SPSS v.19 software was used. Significance level (Sig. level), which represents the probability of the estimated empirical characteristic, was used for estimation. Descriptive analysis was used, non-parametric methods were applied- Kolmogorov-Smirnov Test; Shapiro Wilk test to test the null hypothesis and determine the type of distribution of values, Jonckheere-Terpstra test- to assess the relationship between ordinal trait and ordinal/continuous trait, Wilcoxon-Mann-Whitney test to assess the relationship between categorical trait with two variables and ordinal/continuous trait and Pairwise Comparisons test. Correlation analyses - Chi-square analysis (ChiSquare), Kaplan-Meier Test for

survival, for probabilistic survival the tests- Log-Rank; ROC analysis, regression analysis etc. were used. Microsoft Office (Excel) for Windows 10 was used for graphical and tabular method to present the obtained results

The material and the methods used allow for the formulation of precise and concrete conclusions and to outline the contributions of the dissertation.

In the chapter "Results," **Temenuzhka Rumenova Radeva- Petkova, MD** presents her own data from the study on 65 patients. The description of the results corresponds to the aims set and is supported by extensive graphic and tabular material.

The "Discussion" chapter shows the dissertation's ability to thoroughly analyze, synthesize, and summarize her own results and draw logical conclusions. The studies and analyses performed by **Temenuzhka Rumenova Radeva- Petkova, MD** have practical value and show that the treatment of patients with rectal cancer in the country follows the main international standards.

The conclusions are 8 in total and reflect the results obtained. They are logical, precise, and clear, with a conclusive and analytical nature.

I accept the 9 contributions presented in two directions: original and scientifically applied in nature. Most of them are unique, researched, and established for the first time in the country.

The main hypothesis of the thesis, that *"HMGB1 serum concentration before and after neoadjuvant chemoradiotherapy in the serum of patients with locally advanced rectal cancer are relevant for treatment outcomes"* was confirmed.

The main practical implication of the work is that higher concentration of HMGB1 marker after neoadjuvant chemoradiotherapy are associated with poor response to the therapy and, accordingly, this would require a more aggressive approach in these patients.

The dissertation summary is presented in a volume of 72 pages and contains the main chapters of the dissertation thesis.

The author has published 3 publications and 4 participation in a scientific forum in the country with a presentation were made.

The research conducted shows that the scientific activity of **Temenuzhka Rumenova Radeva- Petkova, MD** fully covers the evaluation criteria for the defense of the educational and scientific degree "PhD" of the Medical University of Vama.

All of the above gives me reason to claim that this dissertation thesis is relevant with practical contribution and unique in its essence. I hope that the evaluations, conclusions, and recommendations in the dissertation will find application in oncological practice in the country.

In conclusion, I can say that the topic is dissertable, the methods used are adequate to achieve the aim and tasks, the results are significant and well reflected in the conclusions, and the contributions are significant.

The scientific paper submitted to me for review: "INVESTIGATING THE EXPRESSION OF NECROTIC CELL DEATH MARKERS AND THEIR PREDICTIVE VALUE IN NEOADJUVANT CHEMORADIOOTHERAPY OF LOCALLY ADVANCED RECTAL CARCINOMA" by Temenuzhka Rumenova Radeva- Petkova, MD possesses all the necessary qualities of a dissertation.

I appreciate the thesis proposed to me for review, and 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.

PROF.IGLIKA SPASOVA MIHAYLOVA, MD, PhD

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