

OPINION

by Associate Professor Hristina Viktorova Lebanova, PhD

Dean of the Faculty of Pharmacy, Medical University – Pleven

Member of the Academic Jury under Order No. R-106-116/05.02.2025

issued by Prof. Dimitar Raykov, MD, DSc, Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, regarding the acquisition of the educational and scientific degree "Doctor"

Subject: Procedure for the defense of a dissertation for the acquisition of the educational and scientific degree "Doctor" in the field of higher education 7. Healthcare and Sports, professional field 7.3 Pharmacy, under the doctoral program Pharmacology (including pharmacokinetics and chemotherapy) by Ivanka Minkova Mutafova – a doctoral student in an independent form of study at the Department of Pharmacology, Toxicology and Pharmacotherapy, Faculty of Pharmacy, Medical University – Varna, enrolled by Order No. R-109-12/07.01.2021.

The dissertation is entitled: "Investigation of Potential Drug Interactions Involving Epidermal Growth Factor Receptor Inhibitors (EGFR Inhibitors) in the Treatment of Non-small Cell Lung Cancer", and has been supervised by Prof. Kaloyan Georgiev, DSc (Pharm), and Prof. Evgeni Grigorov, PhD (Pharm).

By Order No. R-109-116/05.02.2025 of the Rector of the Medical University – Varna, I was appointed as a member of the academic jury. According to Protocol No. 1/14.02.2025, I was designated to prepare an opinion on the procedure for awarding the educational and scientific degree "Doctor" to Ivanka Minkova Mutafova.

The present opinion has been prepared following the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Rules for its Implementation, and the Regulations for the Development of the Academic Staff of the Medical University – Varna, as well as the criteria laid out therein for awarding the degree of Doctor in professional field 7.3 Pharmacy.

I hereby declare that I have co-authored publications with the candidate.

1. Brief Overview of the Procedure

For the present procedure, I was provided with a complete set of materials in both electronic and hard copy formats, following Article 69 of the Regulations for the Development of the Academic Staff of the Medical University – Varna.

Ivanka Mutafova, MD was enrolled as a doctoral student in an independent form of study by Order No. R-109-12/07.01.2021 of the Rector of MU-Varna, under the doctoral program

Pharmacology (including pharmacokinetics and chemotherapy) within the professional field 7.3 Pharmacy.

Following a one-year interruption and subsequent reinstatement of her doctoral studies, the doctoral candidate was officially withdrawn from the program with the right to defend her dissertation, effective as of 05.02.2025, as per the decision of the Departmental Council of the Department of Pharmacology, Toxicology and Pharmacotherapy and the resolution of the Faculty Council of the Faculty of Pharmacy, MU-Varna.

The doctoral candidate has submitted three (3) full-text publications, published in Bulgarian peer-reviewed scientific journals.

2. Biographical Data

Ivanka Minkova Mutafova holds a Master's degree in Medicine from the Medical University – Pleven. Following her graduation, she pursued various postgraduate qualifications and obtained medical specialties in *Internal Medicine* and *Pharmacology* from the Medical University – Sofia.

Her professional career began in 2000 in the field of clinical medicine, after which she transitioned fully into the pharmaceutical industry. Throughout her professional development, Dr. Mutafova has held various positions in university hospitals and in the local branches of international pharmaceutical companies, primarily in the areas of clinical trials and drug safety. Her professional trajectory includes successive roles such as attending physician, specialist physician, clinical trial monitoring specialist, project manager, and drug safety expert.

Dr. Mutafova possesses excellent computer literacy, including experience with specialized software. She is fluent in English and Russian and is a member of the Bulgarian Medical Association.

3. Relevance of the Topic

The dissertation submitted for consideration by Ivanka Mutafova, MD for the acquisition of the educational and scientific degree "Doctor," entitled *"Investigation of Potential Drug Interactions Involving Epidermal Growth Factor Receptor Inhibitors (EGFR Inhibitors) in the Treatment of Non-Small Cell Lung Cancer,"* is an interdisciplinary work focused on drug-drug interactions in clinical practice.

The dissertation comprises 182 standard typewritten pages and is illustrated with 50 figures, 56 tables, and 2 appendices. The bibliography includes 219 sources, of which 17 are in Cyrillic and 202 in English. The dissertation falls entirely within the scope of the doctoral program and the relevant professional field. The content, scope, original research conducted, and conclusions drawn are comprehensive and well-balanced, both in terms of the individual elements and their potential future applications and contributions to the field.

4. Research Methodology

The seven research tasks outlined in the dissertation are aligned with its main objective: to identify and analyze potential drug-drug interactions through the use of a specialized digital platform, and to detect reported adverse drug reactions (ADRs) using dedicated online databases, in the context of clinical application of epidermal growth factor receptor inhibitors (EGFR inhibitors) for the treatment of non-small cell lung cancer (NSCLC).

5. Characteristics and Evaluation of the Dissertation and Its Contributions

The dissertation includes a 69-page literature review covering the various components of the topic, based on 219 contemporary Bulgarian and international sources. The literature review presents a thorough and systematic critical analysis of the clinical characteristics of non-small cell lung cancer, tools used for drug interaction analysis, pharmacokinetics, pharmacogenetic aspects, and the clinical application of EGFR inhibitors.

The sources, materials, and methods employed in the dissertation are comprehensively listed.

The results of the original research are presented in a detailed, coherent, and logically structured manner in Section V of the dissertation. The research tasks have been completed. The study provides in-depth findings related to the assessment of potential drug-drug interactions in the use of EGFR inhibitors. Demographic characteristics of patients are analyzed, as well as possible drug-drug interactions using the UpToDate® Lexidrug™ digital platform, with a focus on high-risk categories X and D.

Data from EudraVigilance have been utilized to assess the frequency and severity of reported adverse drug reactions and their association with identified interactions. The research also examines commonly used medicinal products in clinical practice that have potential interactions with EGFR inhibitors, considering the influence of age, sex, and polypharmacy.

The findings have high applicability to clinical practice and contribute to improved drug safety management.

The doctoral candidate has formulated seven conclusions that correspond to the research tasks and highlight the significance of the study and its potential impact on clinical and regulatory practice.

6. Evaluation of the Publications and the Doctoral Candidate's Individual Contribution

Three full-text publications related to the dissertation topic have been published in Bulgarian scientific journals. In two of the publications, Ivanka Mutafova, MD is the first

author, and in one, she is the sole author. Additionally, she has participated in two scientific forums.

The scientific output of Dr. Mutafova meets both the requirements of the Medical University – Varna and the minimum national criteria for the award of the educational and scientific degree "Doctor."

The doctoral candidate demonstrates a high level of expertise in the subject matter. The research reflects her contribution, is representative at the national level, and enables the formulation of specific recommendations, contributions, and practical applications.

Overall, the presented dissertation for the acquisition of the educational and scientific degree "Doctor" by Dr. Ivanka Mutafova meets the established academic standards, addresses a relevant and timely issue, and serves as a solid foundation for future research in the field.

7. Abstract

The submitted abstract has been prepared following the requirements of the Medical University – Varna and reflects the key results achieved in the dissertation.

CONCLUSION

The dissertation contains original and applied-practical results, which constitute an original contribution to science and meet all the requirements of the **Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB)**, the **Regulations for the Application of LDASRB**, and the **Regulations for the Development of the Academic Staff at MU-Varna**. The presented materials and dissertation fully comply with the specific requirements established in connection with the **Regulations for the Development of the Academic Staff at MU-Varna**.

The dissertation demonstrates that the doctoral candidate, Dr. Ivanka Mutafova, possesses deep theoretical knowledge and professional skills in the scientific field of *Pharmacology*, as well as the qualities and abilities necessary for independently conducting scientific research.

Considering the above, I confidently give my **POSITIVE evaluation** of the research presented in the reviewed dissertation, abstract, achieved results, and contributions, and I recommend to the esteemed academic jury the awarding of the educational and scientific degree "Doctor" to Dr. Ivanka Minkova Mutafova in the doctoral program *Pharmacology (including pharmacokinetics and chemotherapy)*.

April 7th, 2025
Pleven

Prepared by

/Assoc. Prof. Hristina Lebanova, PhD/

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