

TO THE CHAIRMAN
OF THE SCIENTIFIC JURY
DETERMINED BY AN ORDER
№ 15-05-82/27.03.2025 Г.
OF THE EXECUTIVE DIRECTOR
AND THE PROCURATOR OF THE
"ACIBADEM CITY CLINIC UMBAL
TOKUDA" EAD
PROF. KIRIL DRAGANOV, PHD, PHD

REVIEW

by Prof. Dr. Zdravka Gardeva Vasileva - Valerianova, MD, PhD
UNIVERSITY HOSPITAL FOR ACTIVE TREATMENT OF ONCOLOGY "PROF.
IVAN CHERNOZEMSKI" EAD, SOFIA. SOFIA

Elected as a member of the Scientific Jury with the above-mentioned Order and appointed as an external reviewer, according to the decision of the first non-attendance meeting of the Scientific Jury.

Subject: Competition for "PROFESSOR" in the scientific specialty "Oncology" with code 03.01.46 in Field of Higher Education 7 "Health and Sports" and Professional Field 7.1 "Medicine", for the needs of the Clinic of Medical Oncology at "ACIBADEM CITY CLINIC UMBAL TOKUDA" EAD, Sofia, announced in State Gazette, No. 12/ 11.02.2025 and in accordance with the requirements of the Law on Oncology, the Law on the Development of the Academic Staff of the medical institution, with the only candidate for the academic position - Assoc. JELIAZKO ILIEV ARABADJIEV, MD, PhD

Upon reviewing the submitted materials for the competition, it is found that all regulatory requirements and regulations have been complied with. The candidate's documents are comprehensive and in full compliance with the Law on Admission to Participation in a Competition for the Academic Position of Professor in the Clinic of Medical Oncology of UMBAL Tokuda EAD.

Dear Mr. Chairman,

Dear members of the Scientific Jury,

Assoc. Prof. Dr. Jeli azko Arabadjiev graduated from the Medical University "Prof. Dr. Paraskev Stoyanov", Sofia. Varna in 1997. He has acquired a specialty in Medical Oncology in 2014 and a Master's degree in Public Administration, specialty in Health Management in 2012.

He defended his dissertation on the topic "Predictive and prognostic value of tumor-infiltrating lymphocytes in women with breast cancer" and acquired the scientific and educational degree of "Doctor of Medicine". In 2021 he was awarded the title of "Associate Professor of Oncology". In the period 2008-2014 he worked at the University Hospital for Active Treatment "Prof. Ivan Chernozemski" EAD, and since 2015 in the Department of Medical Oncology at ACIBADEM CITY CLINIC UMHAT TOKUDA EAD. Since 2018 he has been the Head of the Clinic of Medical Oncology.

Ass. Dr. Arabadjiev works in the field of medical oncology and simultaneously with his direct clinical activity he is constantly improving his qualifications. He has attended a number of specialized courses and Master Classes, as follows: MasterClass – Modern Treatment of Breast Cancer, Tokuda Hospital, Sofia; European School of Oncology, MasterClass Breast Cancer, Sofia; specialization in Current management of Breast cancer Institute Bordet, Brussels, Belgium; specialization in Management of Thyroid Cancer, Universita di Pisa, Italy; Harvard Medical School, Course in Immuno-Oncology with Certificate, etc.

He is a member of: Expert Board on Medical Oncology to the Minister of Health in the Republic of Bulgaria; Board of the Cancer Mission, European Commission; Subgroup "Joint Clinical Assessment", at the Directorate for Health and Food Safety, European Commission; Representative of the Republic of Bulgaria in the European Breast and Colon Cancer Initiative (EIBC&EICRC) at the European Commission; Chairman of the Bulgarian Scientific Society of Immuno-Oncology; Chairman of the Board of the Institute for Research on the Treatment of Breast Cancer; Chairman of the State Examination Commission for the specialty "Medical Oncology"; Central Ethics Commission of the BMA; European Society for Medical Oncology (ESMO); American Association for Clinical Research (AACR); General Medical Council (GMC) in the United Kingdom, Specialists Registrar and many others.

He is fluent in English, level C1 and Russian, level B1-2.

The scientific interests of Assoc. Prof. Arabadjiev are in the field of clinical trials, drug treatment of breast cancer, urogenital tumors and head and neck cancers, cancer immunotherapy, drug toxicity, as well as European policies in the field of oncology and funding of EU projects - Horizon Europe, EU4Health, Digital Europe. He is the principal investigator and sub-investigator in 21 global clinical trials, Phase II-IV for breast cancer, lung cancer, prostate cancer, colon cancer, ovarian cancer, hepatobiliary tract cancer.

In this competition for the academic position of "Professor" the candidate participates **with 68 scientific papers, 67 of which are after being awarded the title of "Associate Professor"**, as follows: 1 dissertation; 4 textbooks for oncologists and specialized doctors; 14 publications in scientific journals, refereed and indexed in world-famous databases with scientific information -

4 in Bulgarian editions and 10 in international ones; 24 publications and reports in non-refereed journals with scientific peer review or published in edited collective volumes; 26 reports and announcements presented at scientific forums – 1 with a summary and 9 without published abstracts in international forums and 15 national (1 of them with a published abstract). Of the **42 published scientific articles and textbooks subject to peer review**, 31 are in Bulgarian journals (**4 in refereed and indexed in the Scopus database and with impact factor**) and 10 in international scientific journals indexed in the Scopus database, of which **6 with an impact factor**. The total IF of the candidate amounts to 21.

Of the scientific publications submitted for review, 26 Assoc. Prof. Arabadjiev is an independent and first author (68.4%), in 6 he is a second author, in 6 he is a third and subsequent author and co-author in ^{the} 4 textbooks.

Assoc. Prof. Jeliazko Arabadjiev participates in **four scientific projects**:

1. International:

1.1. *MDT Aid Program in Lung Cancer*, in which he is the chief coordinator for Bulgaria with the participation of more than 40 countries from Europe, the USA and China;

1.2. *INTERACT EUROPE100 of the European Cancer Organization*, funded by the European Commission, which includes 100 of the best cancer centers in Europe for training in the field of oncology.

2. National:

2.1 *Study of autoantibodies potentially associated with immune-related adverse drug reactions in patients with non-small cell lung carcinoma enrolled in therapy with immune checkpoint inhibitors* of MU-Sofia, which started in 2024 for a period of 12 months;

2.2. *Study of PIK3CA mutations in Bulgaria and a scientific survey* completed in 2019.

Ass. Arabadjiev is the initiator and author of the training module "Scientorium juvenorum" - a summer school for immunologists and oncologists.

A total of 163 citations are **documented in the databases, from the presented citation reference of the Central Library at the Medical** University of Sofia, of which in foreign sources Scopus – 52 and Web of Science – 49. 62 citations in sources from the library fund of the CMB have also been found.

The presented scientific developments are extremely relevant, with significant scientific interest and great practical contribution. In them, Assoc. Dr. Arabadjiev shows in-depth scientific and practical knowledge and ability to synthesize and generalize matter.

The publications with which the candidate participates in the competition reflect his innovative scientific research and practical and applied activities, which are focused on the following areas affecting significant and topical problems of oncology in Bulgaria and abroad:

1. **Breast Carcinoma** - A dissertation that examines the predictive and prognostic value of tumor-infiltrating lymphocytes (TILs) in women with breast cancer is presented. The study focuses on the degree of lymphocytic infiltration and its relationship to survival and response to treatment. For the first time in Bulgaria, a study of the dependence of overall survival and the degree of tumor-infiltrating lymphocytes in female breast cancer

has been conducted. The results obtained determine the possibility of forming an exemplary algorithm for assessing the impact of the degree of TILs on the prognosis of patients, as well as its application in clinical oncology practice. The development contributes to a new vision in the field of breast cancer treatment and has a scientific-theoretical and scientific-practical meaning. The frequency, role and therapeutic behavior of breast cancer patients in metastatic stages, in which a mutation in the PIK3CA gene is detected, has been studied. This is a contribution of scientific-theoretical and scientific-practical importance, suggesting a more accurate determination of the treatment of patients with PIK3CA mutation in Bulgaria. New drug options for the treatment of HR+ HER2-negative breast cancer have been studied. The contributions of the development are of scientific and theoretical importance and allow for a better theoretical knowledge of the specifics of abemaciclib and ribociclib, as well as the follow-up of their treatment in dynamics. Various aspects in the morbidity, diagnosis and treatment of triple-negative breast cancer (TNBC) are considered, suggesting a more targeted and personalized treatment of TNBC and a change in the prognosis for patients with this disease.

2. **Lung carcinoma** – The results of a review of literature sources for patients with concomitant idiopathic pulmonary fibrosis and adenocarcinoma of the lung are presented. Contributions in this field are of scientific-theoretical and scientific-practical importance and present new therapeutic options for treatment with nintedanib, as well as changes the prognosis of patients with concomitant idiopathic pulmonary fibrosis and lung cancer. Data on improved efficacy and prolonged survival in patients with advanced lung cancer are presented, who receive treatment based on the outcome of EGFR, ALK, ROS1 and KRAS12G mutations that have an impressive overall survival rate many times higher than that described by cytostatics alone. Data on the prognostic role of markers for systemic inflammation – Khorana score, ALI score and others – in patients with advanced lung cancer treated with immunotherapy are also presented. These indices and scales have prognostic and predictive value in assessing response to treatment in patients with metastatic lung cancer receiving immunotherapy. The specific gastroenterological manifestations of immunorelated toxicity from the use of immune checkpoint inhibitors are also described and recommendations for its therapeutic control are given. The contributions are of scientific-theoretical and scientific-practical importance and increase the knowledge of the new therapeutic options in the personalized treatment of lung cancer and the specifics of the manifestations of drug toxicity and suggest their more correct application.
3. **Immuno-oncology** – Data are presented on immunological, neurosurgical and oncological aspects of glioblastoma multiforme disease and on the role of cell death in maintaining tissue homeostasis, as well as its connection with the tumor system. Contributions in this field are of scientific and theoretical value, providing more information about the rare and unfavorable prognosis disease glioblastoma multiforme, which suggests the search for new diagnostic approaches, including the study of paraneoplastic antibodies and treatment.

4. **Cutaneous melanoma and non-melanoma skin carcinomas** – The results of modern clinical trials in these localizations of new medicinal products are reviewed. The data are from various randomized clinical trials of targeted drugs and immunotherapy, as well as from the actual clinical practice in Bulgaria for the period 2018–2022 on the use of dabrafenib and trametinib in BRAF mutated patients in combination, for the treatment of malignant melanoma. The results showed that the real overall survival and progression-free survival were superior to those of clinical trials, especially against COMBI-d. The contributions are of scientific-theoretical and scientific-practical value and can be used in scientific activity or clinical oncology practice by medical oncologists, dermatologists and pharmacoeconomists.
5. **Modern treatment of malignant tumors in the gastrointestinal tract** – The results of modern clinical trials of immune check-point inhibitors in hepatocellular carcinoma are reviewed. The optimal drug sequences of first, second and subsequent lines of therapy in advanced disease are described, and the benefit of using the medicinal product atezolizumab in combination with bevacizumab is reported. esophageal and gastroesophageal junction of immune checkpoint inhibitors, in combination with chemotherapy or alone, depending on PDL1 expression. The application of targeted therapy with entrectinib, specifically targeting tumor cells, including those in the GLI, with the presence of NTRK-fusions, is described. The overall diagnostic and clinical behavior of pancreatic ductal carcinoma is considered, and some experimental approaches to the application of immunotherapy in the disease are also reflected. The contributions are of scientific and practical value, and change the previously used chemotherapy-based regimens. They define a new approach based on immunotherapy and chemotherapy, which is reflected in national standards and guidelines.
6. **Tumors of the urogenital system** – in this area, the use of immune checkpoint inhibitors in renal cell carcinoma and the comparative application of the combination of nivolumab with ipilimumab and cabozantinib are considered. An analysis of the available modern literature on the use of immune checkpoint inhibitors – pembrolizumab and others – in bladder cancer has been carried out. A variety of therapeutic approaches for different stages of prostate cancer are considered. The contributions are in scientific-theoretical and scientific-practical application.
7. **Common Perspectives in Oncology and Cancer Patient Care** – The European priorities in the field of cancer control, enshrined in the Heidelberg Manifesto for Oncology Research, are presented. The results are of scientific, theoretical and practical value and create conditions for more effective measures in the fight against cancer at European and national level. An analysis of the possibilities for identifying barriers to screening, diagnosis and treatment of patients with oncological diseases in Bulgaria has been carried out, and recommendations have been made for the optimization of the patient's path and the timely start of treatment. The definition of the term "adherence to therapy", determining the extent to which the patient's behavior and actions correspond to the prescribed therapeutic regimen in terms of time, dose and frequency. A two-stage

study was conducted in order to identify the factors influencing therapy from the point of view of hospital oncology pharmacists in the country. The results show that the main barriers to adherence to anti-cancer therapy are the occurrence of side effects and the lack of confidence in treatment.

8. **Training of students, postgraduates and specialists** – Assoc. Prof. Dr. Arabadjiev is the author and co-author of clinical manuals, textbooks and patient manuals, innovative in their nature and content. For the first time, the immunotherapy textbook "Compendium for Immunotherapy in Solid Malignant Tumors" is published, which presents in a structured way the main representatives of the immune checkpoints and the available therapeutic indications for their application in the country. The "National Medical Standards for Systemic Drug Treatment, Assessment of Therapeutic Effect and Follow-up of Malignant Solid Tumors in Adults" for the first time in the country provides recommendations to clinicians for behavior in case of adverse drug reactions from the administration of immune-checkpoint inhibitors, ways to manage drug toxicity and recommendations for adaptation of treatment. A practical guide to medical oncology under the GRADE system, dedicated to pancreatic cancer, has been published, which provides specific clinical and practical recommendations for treatment based on evidence-based medicine. The contributions are of a scientific and practical nature and allow clinicians in the country to argue for the choice of a therapeutic strategy for their patients.

The teaching activity of Assoc. Prof. Dr. Zh. Arabadjiev is related to teaching medical students. He is a part-time lecturer at the Faculty of Medicine of Sofia University "St. Kliment Ohridski", Kliment Ohridski", Department of Propaedeutics of Internal Medicine. For the period 2020-2024. Ass. Dr. Zh. Arabadjiev has realized 564.5 hours of total academic and classroom workload, incl. and in English. He participates in conducting basic lecture courses for postgraduate students in Medical Oncology, as well as in their practical training. He is the head of the specialization in "Medical Oncology" of four postgraduates, two of whom have successfully graduated. The candidate is a supervisor of two PhD students, one of whom has successfully defended his dissertation. Ass. Arabadjiev is chairman of the State Examination Commission for the acquisition of the specialty "Medical Oncology". The attached reference from the "Training Department" of "ACIBADEM CITY CLINIC UMHAT TOKUDA" EAD, Sofia shows that for the period January 2020 – December 2024 Assoc. Prof. Dr. J. Arabadjiev has realized 1,447 academic hours with postgraduates.

The provided Reference for compliance with the minimum national criteria for occupying the academic position of "Professor", Field 7. Health and Sports, Professional field 7.1. Medicine

of Assoc. Prof. Dr. Jeliazko Arabadjiev, Ph.D., shows that the minimum national requirements for occupying the academic position of "Professor" have been met and even exceeded.

1. **Indicators from Group A – cover 50 points** and include a defended dissertation. Proof provided.
2. **Indicators from Group B – 113.61 points are covered, while 100 are required.**
3. **Indicators from Group G –** publications from 38 scientific articles in periodicals and full text are presented, after occupying the academic position of Associate Professor. 12 of the publications are in English and 26 are in Bulgarian. In this group of indicators, Assoc. Prof. Dr. Arabadzhiev has **413.5 points**, out of the required **200**.
4. **Indicators from Group D –** the total number of points from citations are included. **1055 points** have been achieved , while **100 are required**. A list and evidence for citations of publications after acquiring the academic position of Associate Professor are attached. The total number of **citations is 163**. Of these, **101** are Bulgarian and **62** citations in international journals in the Scopus and Web of Knowledge databases. A reference from the Central Medical Library at the Medical University, Sofia, is attached. Sofia, excluding self-quotes.
5. **The total Impact factor is 21.**
6. **Indicators from Group E - 162.9 points have been achieved , with 100 points required.**

Conclusion: As a result of the above, I am deeply convinced and extremely impressed by the professionalism and scientific achievements of Assoc. Dr. Jeliazko Arabadjiev. He is an accomplished specialist in oncology and medical oncology, a researcher with innovative thinking and a significant contribution to the development of science in the country, and in particular in the field of diagnosis, treatment, immuno-oncology and care for cancer patients in the main cancer localizations. Ass. Dr. Jeliazko Arabadjiev is an established scientist, researcher-practitioner, lecturer and lecturer with established authority in the oncology community and recognized scientific achievements in Bulgaria and abroad. He is one of the leading specialists in medical oncology in the country; a person with high erudition, collegiality and proven creative capabilities and qualities.

I am deeply convinced and believe that Assoc. Prof. Dr. Jeliazko Iliev Arabadjiev exceeds all the necessary requirements and criteria, as well as the quantitative scientometric indicators for the academic position of "Professor" of the Law on the Promotion of Professors and the Regulations for the Development of the Academic Staff of "Acibadem City Clinic University Hospital Tokuda" EAD. The scientific jury to vote unanimously for awarding the academic position of "Professor" to Assoc. Zhelyazko Iliev Arabadzhiev, MD, PhD

13.05.2025

Sincerely,



/Prof. Zdravka Valerianova, MD, PhD/