

## STATEMENT

by Prof. Antonij Tonchev Filipov, M.D., Ph.D.,

member of the Scientific Jury, assigned by

Order Nr RD-1323/30.05.2022

UMHATEM “N.I.Pirogov”, Sofia

Concerning:

procedure for awarding the educational and scientific Doctoral degree (Philosophy doctor)  
to Todor Yuriev Dzhendov M.D., for a dissertation paper on

**“Multimodal approach in the treatment of esophageal carcinoma. Prognostic and  
predictive markers.”**

in scientific specialty **“Thoracic surgery”**

in professional direction 7.1 **Medicine**

in the field of higher education 7. **Healthcare and sports**

### **Biography**

### **Education**

Todor Yuriev Dzhendov M.D. graduated from Medical University Sofia in 2007 and obtained professional qualification “Master”. After that, he successively acquired two medical specialties – “Thoracic surgery” in 2014 and “Surgery” in 2017. He has attended a number of specialized courses in the field of endoscopic surgery, emergency medicine, Damage control, minimally invasive esophagectomy, gastro-esophageal oncological surgery, microsurgery, etc. Dr Dzhendov holds also a second master degree in “Health Management”

## **Professional experience and skills**

Dr Dzhendov has 14 years of experience in the field of medicine. He has started his career in 2008 as a resident in Tokuda Hospital, Sofia. In 2010, he began his specialization in “Thoracic surgery” in UMHATEM “N.I.Pirogov”, Sofia. As a specialist, he starts working at the University Hospital in Linköping, Sweden in May 2016. Meanwhile, he acquired a second specialty in “Surgery”. He speaks Swedish, English and French and is a member of a number of professional societies, including Bulgarian and Swedish surgical societies, The European Association for Cardiothoracic Surgery, The European Society of Thoracic Surgeons and The European Association of Endoscopic Surgery.

## **Dissertation paper**

The topic of Dr Todor Dzhendov’s dissertation is “Multimodal approach in the treatment of esophageal carcinoma. Prognostic and predictive markers”. The doctoral candidate makes a detailed and clear analysis of esophageal carcinoma as one of the most significant and difficult to treat contemporary oncological diseases. Significant differences in the different geographical regions of the world, as well as in the survival rate of the patients are observed.

For example, the five-year survival rate in Bulgarian patients is significantly lower than the average value for Europe and the USA. One of the most significant tasks of the paperwork is focused on the possibilities for better survival of the patients by introducing a systemic approach in the treatment with smooth functioning of all separate stages and parts of treatment. A multimodal approach, combining operative intervention (esophagectomy) with neoadjuvant and/ or adjuvant oncological therapy in the form of chemotherapy or chemoradiotherapy is recommended in all patients who can tolerate such a treatment method.

The aim of the selected groups of patients, together with their follow-up in accordance to specific criteria, is to evaluate the current methods for the treatment of esophageal cancer and, together with this, to define important prognostic markers to achieve optimization of the therapeutic protocol. Six main tasks are clearly outlined, which are fulfilled in the process of developing the dissertation work and lead to the fulfillment of the set goal:

1. To carry out an ambispective analysis of the results of the treatment of patients with carcinoma of the esophagus operated in the Surgical departments of two university hospitals in two European countries.
2. Comparison of the results in the analyzed samples and correlation with the literature data.
3. Finding a correlation between choice of therapeutic protocol and survival.
4. Analysis of prognostic markers for survival.
5. Genetic analysis of tumor samples in part of the patients.
6. Preparation of a recommended therapeutic protocol according to the histological type and stage of the tumor.

The dissertation work consists of 146 pages, including a bibliographic reference containing 301 literary sources. 33 figures and 14 tables were used for additional graphic presentation. It is formatted without notes. The material, on which the study is based, has derived from the results of the treatment of patients operated for carcinoma of the esophagus and the gastro-esophageal junction in the surgical clinics of two university hospitals – First Surgical Clinic, UMHATEM “ N.I.Pirogov”, Sofia, Bulgaria and Clinic of Surgery of University Hospital, Linköping, Sweden.

The importance of staging for the course of the treatment is clearly noted, with the help of which the type of esophageal carcinoma can be diagnosed as well as possible. Two main systems are indicated – TNM and JES. The individual types and stages, the anatomic spread of the tumors, their localization, histological type, etc are described and classified in great detail. Central attention is given to the multidisciplinary approach in the treatment of esophageal carcinoma, along with the application of a multimodal therapeutic regimen, which significantly improves treatment outcomes because it combines radiotherapy, chemotherapy and surgical resection.

The first studied group in the dissertation work includes 129 patients operated for carcinoma of esophagus and gastro-esophageal junction in First Surgical Clinic, UMHATEM “N.I.Pirogov”, Sofia, Bulgaria. The covered period is three years – from 2013 to 2015.

The second group consists of 115 patients, operated in the Clinic of Surgery, University Hospital, Linköping, Sweden in a longer period of seven years – from 2010 to 2017. An ambispective analysis is performed, and while in the first group there are excluded patients based on an established advanced metastatic tumor process, there are no exclusions in the second group.

There are also differences in the choice of operative methods in the two groups. The demographic, clinical and pathohistological characteristics of the two groups are shown in detail in a table. Predominant histological variant in both groups is adenocarcinoma. A significant difference in survival was reported in the two groups, as for The Bulgarian cohort, the three-year survival rate was 12.8%, and the five-year survival rate was 11.1%. In the Swedish cohort, the values were 53.04% three-year survival and 43.5% five-year survival.

The doctoral student draws 6 conclusions from his research:

1. In the treatment of patients with carcinoma of esophagus and gastro-esophageal junction, the multimodal therapy provides significantly better survival compared to surgery as a single therapeutic method.
2. When choosing oncological therapy, two alternatives are available that achieve the same results – neoadjuvant chemoradiotherapy (CROSS protocol) or perioperative chemotherapy (FLOT protocol). However, in esophageal squamous cell carcinoma, the inclusion of radiotherapy is desirable due to the higher radiosensitivity of this histological type.
3. Tumor staging is performed according to the latest 8<sup>th</sup> revision of the TNM classification, which is consistent with the histological type and the neoadjuvant therapy performed.
4. Along with TNM stage, additional statistically significant predictive markers such as tumor length over 3 cm, ratio of metastatic to total number of dissected lymph nodes over 10 %, microscopically non-radical resection, presence of comorbidities are available to determine patients prognosis. Secondary prognostic indicators are young age, male gender and squamous cell carcinoma.
5. In the presence of negative predictive markers, an aggressive therapeutic protocol is recommended with the addition of adjuvant oncological therapy.

6. HPV infection is not a factor in the etiopathogenesis of esophageal carcinoma in the Bulgarian population.

The main contributions of the dissertation work are the analysis of modern methods of treatment of esophageal carcinoma, derivation of treatment methods in the earlier tumour stages without surgical resection, the collected data from the study in two university centres, reporting important data about survival and the derivation of additional prognostic results related to survival, the consideration of the important role of the perioperative oncological therapy. Last, but not least, the value of the derived therapeutic algorithm, tailored to the histological type and stage of the tumour, should be noted.

The DNA data collected from the Bulgarian patients group, which is stored at the Centre for Molecular Medicine at the Medical University – Sofia, can be useful for future clinical studies.

The doctoral student has submitted as related to his work publications two articles, one independent and one co-authored, and one report published in a collection of reports.

In conclusion, I think that

the dissertation work of Todor Yuriev Dzhendov M.D. “Multimodal approach in the treatment of esophageal carcinoma. Prognostic and predictive markers” shows a thorough and serious approach to the study of this contemporary disease and succeeds in deriving a useful and significant multimodal therapeutic protocol tailored to each individual stage in adenocarcinoma and squamous cell carcinoma of the esophagus. The Doctoral student shows professional training and qualities that give the present study an indisputable scientific value.

For these reasons and because the dissertation work fully meets the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Regulations for the Development of the Academic Staff at UMHATEM “N.I.Pirogov”, Sofia I confidently and without hesitation recommend to the members of the respected Scientific Jury to award the educational and scientific degree “ Philosophy doctor” in the scientific specialty “Thoracic Surgery” to Todor Yuriev Dzhendov M.D.

With respect,

Prof Antonij Filipov, M.D., Ph.D.