



**МладОнколог**

*Challenges  
&  
Controversies  
in Medical  
Oncology*

**Sunny Beach, May 17-20, 2018**



An impressionistic painting of a sunset or sunrise over a body of water. The sky is filled with vibrant, layered colors: bright yellow and orange near the horizon, transitioning into deep blues and purples higher up. A large, glowing yellow sun is partially obscured by a thick, horizontal band of dark blue and purple clouds. The water below reflects the colors of the sky, with soft, blended strokes of yellow, orange, and blue. The overall style is expressive and painterly, with visible brushstrokes and a rich, textured appearance.

# *Programme*

## May 17, Thursday

14.00 – 19.00	Accommodation and Registration
19.00 – 22.00	Dinner

## May 18, Friday

09.30 – 09.40	Opening Ceremony – R. Krasteva
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### FIRST PLENARY SESSION – LUNG CANCER

Moderators: N.Chilingirova & R. Djupanova

09.40 – 10.00	EGFR tyrosine kinase inhibitors in the adjuvant therapy of completely resected NSCLC – R. Pirker
10.00 – 10.20	Advanced NSCLC: medical management from unselected flooding to precision therapy – Chr. Manegold
10.20 – 10.40	Management of SCLC – K. Botsolis
10.40 – 11.00	Immunotherapy in Lung Cancer – S. Baka
11.00 – 11.20	Lung Cancer Screening - Challenges and Unsolved Issues – W. Voigt
11.20 – 11.40	Coffee Break
11.40 – 12.00	How to stay motivated and calm in stressful situations at work – A. Juškevičienė
12.00 – 12.20	Anti-PDL1 immunotherapy with atezolizumab in NSCLC – “all comers” – A. Konsoulova
12.20 – 12.40	Osimertinib – clinical trials results in patients with T790M mutated NSCLC and the effect on brain metastasis – N. Tsonev
12.40 – 13.40	Lunch

### SECOND PLENARY SESSION – COLON CANCER

Moderators: Iv. Stoyanova & L.Vasilev

13.40 – 14.00	Diagnostics Biomarkers in Colon Cancer – D. Dimitrov
14.00 – 14.20	Continuum of care for Wild Type RAS Metastatic Colorectal Cancer patients – L. Simeonova
14.20 – 14.40	Role of Stereotactic Body Radiation Therapy (SBRT) in oligometastatic colorectal cancer: An opportunity for cure? – N. Velikova
14.40 – 15.00	Metastatic colon cancer – chemotherapy or immunotherapy – challenges and controversies – T. Zlatanova
15.00 – 15.20	Percutaneous Ablation of Colon Cancer Liver Metastases – J. Genov, R. Mitova
15.20 – 15.40	PET - CT Diagnostics in Colon Cancer: Challenges and Current Issues – J. Mihailovic
15.40 – 16.00	Coffee Break
16.00 – 16.40	Sanofi Genzyme Symposium - Biomarker data utility in tailoring treatment decisions in mCRC Plasma and tissue biomarkers in mCRC: retrospective analyses of the VELOUR trial – I. Tonev mCRC Clinical case 1 – M. Kyoseva; mCRC Clinical case 2 – E. Tazimova

### THIRD PLENARY SESSION – PROSTATE CANCER

Moderator: S. Nedeva

16.40 – 17.20	Astellas Symposium - Changing our approach towards mCRPC and the challenges of the day – R. Krasteva, K. Ivanov
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17.20 – 17.40	Imaging Tests and Staging of Prostate Cancer – P. Getsov; Repositioning current therapeutic options for advanced prostate cancer. Abiraterone acetate (Zytiga®): vision to 2018 – J. Assa
17.40 – 18.00	New treatment option for patients with Metastatic Urothelial Carcinoma - Atezolizumab, the anti-PDL1 Immunotherapy – K. Kalacheva
18.00 – 18.20	Nuclear Medicine Approaches in Prostate Cancer – Challenges and Controversies – S. Sergieva
18.20 – 19.20	POSTER SESSION
20.00 – 22.00	Dinner

## May 19, Saturday

### FOURTH PLENARY SESSION – KEYNOTE LECTURES

Moderators: S. Katev & Hr. Spassov

09.30 – 10.00	Personalized Therapy: How to Test Cost-Effectively and Evidence-Based for Predictive Markers – M. Papotti
10.00 – 10.30	Basics in Clinical Statistics – L. Pilz
10.30 – 11.00	Challenges and controversies in breast conserving surgery – G. Zografos
11.00 – 11.20	Supermicrosurgery for Treatment of Postoperative Lymphoedema: What We Know and What We Don't? – Y. Yordanov
11.20 – 11.40	Issues with Anticancer Drug Availability and Access – A. Konsoulova
11.40 – 12.00	Personalized Medicine – What is the Situation in Bulgaria – Y. Drenski
12.00 – 12.15	Coffee Break
12.15 – 13.00	Symposium Eli Lilly - Real experience with Cyramza – R. Krasteva, K. Genova
13.00 – 14.00	Lunch

### FIFTH PLENARY SESSION BREAST CANCER

Moderators: M. Koleva & A. Konsoulova

14.00 – 14.20	PET-CT in Breast Cancer - Challenges and Unsolved Issues – Q. Siraj
14.20 – 14.40	Sentinel Lymph Node Dissection - Challenges and Controversies – D. Pinto
14.40 – 15.00	Screen Detected Cancer - Micro Tumors with Macro Approach. Are we acting or we are hiding? – V. Ivanov
15.00 – 15.20	Management of Pregnant Patients with Breast Cancer: Gynecology Aspects – V. Stoykova
15.20 – 15.40	Breast Cancer during Pregnancy – A. Konsoulova
15.40 – 16.00	Male Breast Cancer – R. Krasteva
16.00 – 16.10	Coffee Break
16.10 – 16.30	Target Therapy of HER 2 Positive Metastatic Breast Cancer – M. Koleva
16.30 – 16.50	Management of Triple Negative Breast Cancer - F. Zagouri
16.50 – 17.50	Boehringer Ingelheim Symposium - The Modern Approach to the Diagnosis and Treatment of NSCLC – M. Gottfried
17.50 – 18.10	Changing the treatment paradigm in HR+/HER2- mBC: The impact of Ibrance (Palbociclib) and the new CDK 4/6 generation – A. Konsoulova
18.10 – 18.50	MSD Symposium - Pembrolizumab - A New Paradigm in Cancer Treatment The New Standard in the Treatment of Advanced NSCLC – N. Chilingirova Metastatic Urothelial Cancer - the Role of PD-1 Inhibitors in the Treatment – A. Konsoulova
20.00 – 23.00	Dinner





**Dr. Rossitza Krasteva**

## **Welcome to the VII International Meeting of Young Oncologist Club - Challenges and Controversies in Medical Oncology**

DEAR COLLEAGUES,

I am pleased to welcome you to our VII International Meeting – Challenges and Controversies in Medical Oncology. We will continue the tradition of the previous meetings of the Club by bringing together marked professionals in the medical field to discuss current problems, to exchange ideas and concepts, to compare perspectives and clinical experience.

We will be focusing on the challenges and controversies in the area of the main solid tumors – of the lung, breast, colon and prostate. Through a format of debates, lectures and panel

discussions, the meeting will provide a forum to effectively address clinical and therapeutic problems as well as innovative diagnostic procedures.

Please feel free to ask questions during and after the sessions. Do not turn off your phones, use them, call your friends, and tell them what we are doing.

I wish you all two fruitful and useful days. Enjoy yourselves and learn as much as you can.

I declare the VII International Meeting of the Young Oncologist Club open!

## Dr. Rossitza Krasteva



Dr. Rossitza Krasteva, the Chairman of Young Oncologist Club, is one of the leading specialists in medical oncology in Bulgaria. She has graduated the Medical University in Sofia in September 1994 and did two specializations after that - Internal Medicine (2001) and Oncology (2005). She also won a number of fellowships for further training in Bulgaria and abroad, as well as attended specialized courses in university hospitals in Italy, Greece, Germany and Switzerland.

All of Dr. Krasteva's professional and scientific interests are in the field of medical oncology. Her career as a medical oncologist includes working at the Clinic of Medical Oncology at the University Hospital Queen Joanna – ISUL, the International Oncology Consulting Center and Serdika Hospital in Sofia. She is currently the Head of Medical Oncology Clinic, Central Bulgarian Comprehensive Cancer Services, Uni Hospital, Panagyurishte. She has been a Principal Investigator and a sub-investigator in several phase II and III clinical trials for adjuvant treatment and treatment of metastatic disease in solid tumors. Dr. Krasteva is a member of Bulgarian Cancer Society, Bulgarian Association of Medical Oncology, The Balkan Union of Oncology, ESMO and ASCO. She was elected the first Chairman of Young Oncologist Club Bulgaria. Dr. Krasteva speaks 2 foreign languages - English and Russian.

## Dr. Ralitsa Djupanova



Dr. Ralitsa Dzhupanova got a degree in Medical Biology in 2010. She has been a lecturer at the Department of Biology at the Medical Faculty of the Medical University in Sofia. She has also specialized in the Anatomy Institute of the University of Cologne, Germany. In 2013, she decided to move from the theory to practice and began a specialization in Medical Oncology. Dr. Dzhupanova has successfully passed courses in abdominal ultrasound and immunological methods in microbiology. She finds her professional challenge in her work at Associate Professor Dr. Valentina Tsekova Oncology Clinic and continues to read, study and work. She has 4 scientific publications, 2 of which international.

Dr. Ralitsa Dzhupanova is a member of a number of research teams on international scientific projects. Currently, she works at Serdika Hospital.





**Dr. Nataliya Chilingirova**

Graduates with remarkable success “Romain Rolland” foreign language school in Stara Zagora, Bulgaria. Studies medicine at the faculty of medicine, Medical University, Sofia. Still at the university starts working as a volunteer at the medical oncology clinics in the National Oncology Centre in Sofia and the Complex Oncology Centre in Stara Zagora. Right after graduating the Medical University starts working and specializing medical oncology at the National Oncology Centre (Specialized hospital for active treatment in oncology). PhD on lung cancer treatment focusing on the new therapeutic approaches and next generation sequencing. Scientific interests in the field of lung cancer research and sarcomas. Sub-investigator in phase I and phase III clinical trials. Completes several trainings in medical oncology in Switzerland and Austria, takes actively part in different international oncology meetings and forums. Member of ESMO, ASCO, Young Oncologist Club Bulgaria and the Educational oncology Academy (Bulgaria). Since 2011 member of the executive board of Young oncologist Club Bulgaria, organizing the international and local educational meetings for young physicians and scientists. Speaks German, English and Russian.




**Prof. Robert Pirker**

## **EGFR tyrosine kinase inhibitors in the adjuvant therapy of completely resected NSCLC**

Patients with early stage non-small cell lung cancer (NSCLC) undergo surgery with curative intent but most of these patients will relapse, both locally and systemically. Adjuvant cisplatin-based chemotherapy increases survival of these patients. The Lung Adjuvant Cisplatin Evaluation meta-analysis demonstrated a survival benefit of  $5.3\% \pm 1.6\%$  at 5 years. Thus adjuvant chemotherapy with a cisplatin-based doublet, preferentially cisplatin plus vinorelbine, has been established as a standard treatment for patients with completely resected NSCLC stages II and III including patients with EGFR mutation-positive disease.

Strategies to improve outcome of adjuvant treatment for early-stage NSCLC include customized chemotherapy, targeted therapies and cancer immunotherapy. Two trials (NCIC CTG BR19, RADIANT) failed to demonstrate a survival benefit for adjuvant therapy with gefitinib or erlotinib in patients unselected for the presence of EGFR



mutations. EGFR tyrosine kinase inhibitors have also been evaluated in patients with EGFR mutation-positive tumors. In a Chinese phase 3 trial in patients with completely resected EGFR mutation-positive NSCLC, adjuvant therapy with gefitinib improved disease-free survival compared to adjuvant treatment with cisplatin plus vinorelbine. However, no survival data have been presented yet. A similar trial is still ongoing in Japan. EGFR tyrosine kinase inhibitors are also evaluated within the ALCHEMIST trial. These trials will determine the role of EGFR tyrosine kinase inhibitors in the adjuvant therapy of patients with completely resected mutation-positive NSCLC.

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Robert Pirker is currently Professor of Medicine and Program Director for Lung Cancer at the Department of Medicine I, Medical University of Vienna, Austria. He obtained a master's degree in Biochemistry in 1978 and his medical degree in 1979 from the University of Vienna. Robert Pirker trained in Internal Medicine, Hemato-Oncology and Nuclear Medicine at the University of Vienna. He also worked as NIH Visiting Fellow at the Laboratory of Molecular Biology (Chief: Dr. Ira Pastan), National Cancer Institute, Bethesda, MD, USA (1983-86).

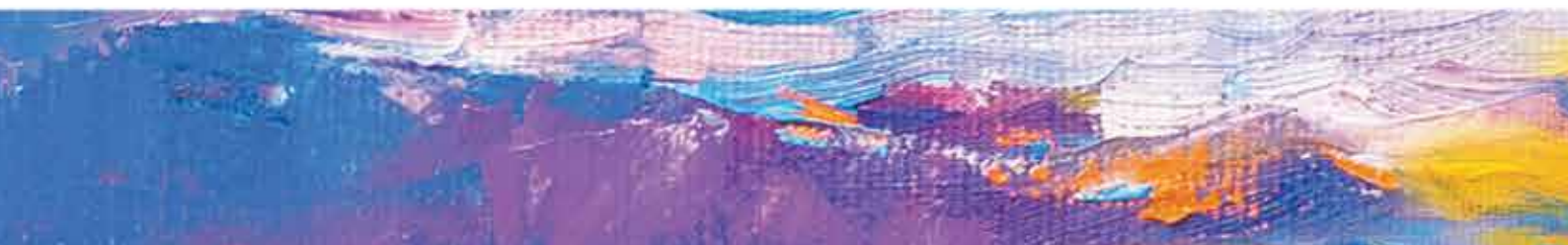
His research interests are chemotherapy and targeted therapy of lung cancer, drug resistance mechanisms of cancer, and management of chemotherapy-induced anaemia. He has published more than 170 articles, reviews or book chapters. He has been an ESMO Faculty Member on Chest Tumors and a member including chair of the IASLC Education Committee. He is a current member of the IASLC Board of Directors. He was Congress President of the 8th and 14th Central European Lung Cancer Congresses, Chair of the Scientific Committee of the European Multidisciplinary Conference on Thoracic Oncology in 2009, and Conference President of the IASLC 17th World Conference on Lung Cancer in 2016 in Vienna, Austria.

## Prof. Christian Manegold


### **Advanced non-small cell lung cancer: medical management from unselected flooding to precision therapy**



During the past two decades diagnosis and therapy of NSCLC has significantly advanced by not only becoming increasingly complex through multi- and interdisciplinary nature, innovative imaging, molecular and immunology-based laboratory testing, and a fast growing number of therapeutic options, but also by opening doors for management preci-








sion and individualizing and personalizing therapies. Unselected treatment flooding has been the typical chemotherapeutic approach 20 years ago. Platinum-based doubled therapy was the treatment standard for unselected patients using different partners of Cisplatin such as the taxanes, the vinca-alkaloids, or Gemcitabine, and subsequently Pemetrexed as the preferred option for non-squamous tumors. First-line therapy was further modified according to tolerability, co-morbidity, patient age, performance status, and patient expectations. New strategies have been implemented. Docetaxel was the first agent registered for second line therapy and later on challenged by Pemetrexed, Erlotinib as well as the combinations of Nintedanib/Docetaxel and Ramucirumab/Docetaxel. Continuation (Pemetrexed) and switch (Pemetrexed, Erlotinib) maintenance therapy has been implemented and the extension of induction therapy beyond 4-6 cycles by Bevacizumab for patients with non-squamous tumours as well as by Necitumumab in combination with Cisplatin/Gemcitabine for squamous tumours has been implemented. The traditional first and subsequent line therapy for wild-type tumours has been recently very successfully challenged by novel immunotherapy approaches (checkpoint inhibitors). In mutant tumours, according to the current algorithm, treatment selection is carried out based on the molecular profile of the tumour (ALK, EGFR, ROS 1), at the same time making targeted therapy the treatment of choice in the first line setting since it improves survival over standard chemotherapy. Because of the fast growing understanding of tumour biology, it can be expected that treatment precision for advanced NSCLC will further increase as lately shown by the implementation of targeted agents against resistant mutations.

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Dr. Christian Manegold, studied medicine in Berlin and Heidelberg, Germany, graduating with a Dr. from the Ruprecht Karls University in Heidelberg in 1974. He took up a residency in the pathology department of the same university in 1976 and worked the USA for 3 years, before returning to Heidelberg in 1979. He gained board certification in internal medicine and in haematology/oncology in 1985 and 1986, followed by a professional appointment as Consultant in Haematology/Oncology at the Thoracic Hospital in Heidelberg, and Head of Interdisciplinary Thoracic Oncology at the Department of Surgery, Heidelberg Medical Centre Mannheim, Germany, a post he held from 2004 to 2013. He was appointed Professor at Ruprecht Karls University in Heidelberg in 1996. He has been the Senior Advisor at the Interdisciplinary Cancer Centre in Mannheim since 2013. Professor Manegold has extensive experience as a clinical investigator, and national and international trial leader as well as a member or leader of independent data monitoring committees (IDMC) in numerous clinical trials in oncology, both in thoracic cancers and other indications. Professor Manegold is a member of the German Cancer Society, the European Society of Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO), and the International Association for the Study of Lung Cancer (IASLC). He was a Chairman of the European Organisation for Research and Treatment of Cancer Lung Cancer Group (EORTC-LCG) from 2000 to 2003. He served as a Chairman of the IASLC Ethics/Sponsorship Committee from 2007 to 2009 and as member of the IASLC Board of Directors from 2011 to 2015.



## Dr. Sofia Baka



Dr Baka, is Consultant, Medical Oncologist and works at the Interbalcan Medical Center of Thessaloniki, Greece. She is the Director of the Medical Oncology Department-Clinical Research Unit. She has graduated from the Medical School of the Aristotle University of Thessaloniki in 1993, and completed her Specialist Training in Internal Medicine in 2001, at the Hippocraton University Hospital of Thessaloniki.

Following, her PhD, on lung cancer immunotherapy, from the Biology Department of Aristotle University, Medical School, Dr Baka has worked as Clinical Research Registrar and Specialist Registrar in Medical Oncology, for 5 years, at the Christie Hospital in Manchester and completed her Specialist Training in Oncology (CCST). During that time she has attended the Master Course in Oncology, University of Manchester. He has written several papers in major scientific medical journals. Dr Baka has participated as Principal or Co-Investigator in several clinical trials.

## Prof. Wieland Voigt



### Lung cancer screening - challenges and unsolved issues

Lung Cancer has the highest cancer related mortality rate globally. Without screening it is usually detected at advanced stages with overall limited curative potential. Recent studies with low dose CT scans demonstrated a shift towards detection of lung cancer at early stages and thereby to significantly improve overall survival. Based on this data, lung cancer screening with low dose CT is implemented on a national level in the United States with however still limited participation rate. Other nations such as in Europe still await the results of further screening trials such as the Nelson trial to conclude on the implementation and set up of a screening program. However, data already warrant to start planning such programs. Key challenges in the optimal design of a screening program which will be discussed in my presentation are the following: 1) optimal selection of the screening population – what are the relevant criteria for risk definition? 2) optimal timing of lung cancer screening intervals 3) technology requirements for a screening program – CT configuration and radiation dose 4) improving accuracy in nodule measurement – diameter vs. volumetric measurement 5) how to manage screening detected lung nodules at baseline screening and incident rounds. New technologies are currently emerging with the potential to improve patient selection for screening (e.g. exhaled breath testing) or to aid in the discrimination between benign and malignant nodules e.g. based on textural analysis using artificial intelligence. In my lecture I will address the question of how these technologies could be integrated into a screening program set up. As



with other screening programs, the efficacy of a lung cancer screening program is determined by the participation rate. Therefore, the setup of a population based screening program needs to ensure that in particular the high and very high risk individuals will be recruited. Lung cancer screening programs have the potential to impact on health outcomes not just be early detection of lung cancer but also by counselling participants to quit smoking. This will ultimately reduce the risk of several additional smoking related diseases such as further cancer types or cardiovascular diseases.

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Professor Voigt studied medicine at the Medical University in Hannover and Martin-Luther-University in Halle/Wittenberg, Germany. After graduation he took an additional 2 years training in molecular tumor biology and pharmacology at Roswell Park Cancer Institute in Buffalo, USA. He continued his career at Martin-Luther-University Halle/Wittenberg and became a board certified specialist for Internal Medicine, Hematology and Oncology as well as Palliative Care. He holds a doctoral degree in medicine and is habilitated for Internal Medicine and Oncology. After 13 years serving in Halle in various leading positions, Professor Voigt took a position as a global Chief Medical Officer at Siemens Healthineers where he in addition serves in a role of a principle key expert. As further expansion of his assignments he was appointed for a professorship at Steinbeis University for Innovation in Oncology as part of the Steinbeis Transfer Institute Medical Innovations and Management.



**Dr. Aurelija Juskeviciene**

## **How to stay motivated and calm in stressful situations at work**

Oncology is often mentioned as one of the most stressful of all medical specialties. The stress in oncology emerges from the complexion of the disease that is being treated. The work involves repeatedly communicating bad news to patients, witnessing patient deaths as well as severe distress and adverse events from treatments and etc. Taken all together these factors can lead to stress and even burnout. A survey published in the J Clin Oncol, 2014, Jul 21 indicated that 43% of oncology fellows report burnout in year 1 of their fellowship, decreasing to 32% in year 2 and 28% in year 3. Almost two out of three young hospital doctors say their physical or mental health is being damaged because of pressures the health care system is putting them under intolerable strain. Even higher rates have been reported — a survey conducted by the European Society of Medical Oncology in



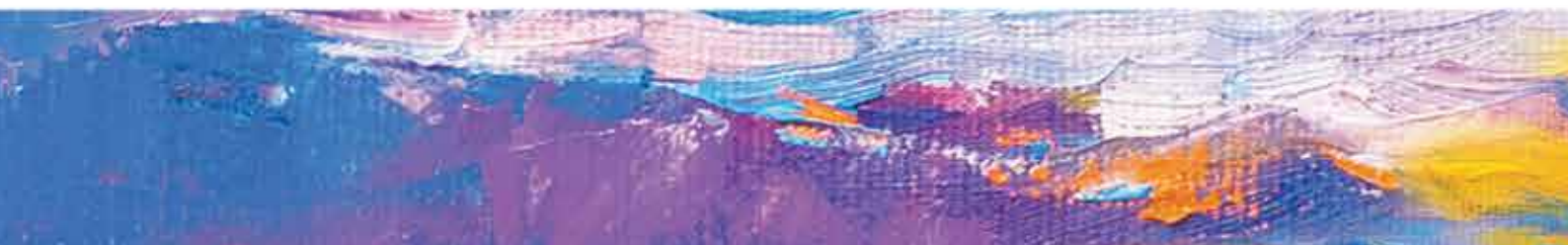
2014 found that 70% of young oncologists reported feeling burned out. And while it can be challenging, learning how to remain calm under stress is a workplace skill that could serve well throughout the career. The purpose of the presentation is inform about several beneficial strategies and certain steps for young oncologists that can be taken to reduce stress, both at the individual and organizational levels according to the handful of articles. During this presentation you will learn how to prevent burnout by rethinking your approach to stress, how you can change your reaction to stressful situations, how to train yourself to manage your reactions to them and take care for yourself. Contrary to popular belief, stress is good for you. If you want to do better, you must be better. Improving significant aspects of your life - physically, mentally, emotionally, and spiritually - will make you happier, increasing your work performance and ability to lead others. Hospitals and health systems cannot afford to ignore physician burnout. Studies have shown that physician burnout influences care safety and quality, as well as physician turnover and patient satisfaction, the researchers write.

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Aurelija Juškevičienė is a native from Vilnius, Lithuania and is “three in one” – Master of Science in Neonatology, Master of Business Administration and International Business Management, Master of Educational Sciences.

Prior to Human Resources Lead in one of the biggest Outpatient Clinic in Vilnius, Aurelija worked as Medical Director in National Cancer Institute (NCI). Previously she has been Country Manager in pharmaceutical company Eli Lilly Lithuania, starting from manager’s position in Oncology Unit also for Baltic States. She was responsible for managing all operations within a country. This involved taking responsibility for profit, revenue, quality targets, agreeing annual budgets and producing a detailed annual business operating plan which resulted in successful growth of business from 13th ranked pharma company in 2007 to 5th ranked company in 2015 in Lithuania. She started her career at Red Cross Hospital in Vilnius, as a neonatologist and she led the Neonatology Department last 5 years of service.

Now she is the Director of Cancer Treatment Foundation (CTF) in Lithuania since 2016 as well. CTF is a non-profit organization which mission is to relieve the financial burden of medical treatment costs for Lithuanian residents who are diagnosed with cancer and can not get the appropriate, but necessary for them, innovative treatment which is not reimbursed by the state in the highest possible transparent way.







**Dr. Assia Konsoulova**

Dr. Assia Konsoulova is a medical oncologist, working at the Medical Oncology Clinic at the University Hospital “Sveta Marina”, Varna, Bulgaria. She is also an assistant in Propedeutics to the Internal Medicine at the English-speaking students at the Medical University in Varna, Bulgaria. Dr. Konsoulova graduated the Medical University in Varna in 2003 and specialized in Internal Medicine and Medical Oncology. She has won internships and attended more than 20 educational courses in Europe. She has more than 40 scientific publications in Medical oncology. She also defended a PhD thesis in 2016 over “Expression of some tissue and plasma biomarkers as potential predictors for antiangiogenic treatment with bevacizumab in metastatic colon cancer”. Apart from being the responsible for the European Initiative in Quality Management in Lung Cancer Care for Bulgaria, Dr. Assia Konsoulova is also a member of the ethical committee at the Society of the Young oncologists in Bulgaria, and the Union of the Quality specialists in Bulgaria. Dr. Konsoulova is also a member of ESMO, ASCO, ECCO, Bulgarian Oncology Society, and the Society of the Young Oncologists in Bulgaria. She has been a member of the scientific research commission the Medical University in Varna since 2004 and a secretary of the first board for neuroendocrine tumors at that university since 2011. Dr. Konsoulova specialized in the Friedrichstadt City Hospital in 2003, Dresden, Germany. She worked as an assistant in Medical Oncology in 2005-2006 and 2007 at the Jules-Bordet Institute as a specialist in the Brussels Free University of Belgium with a scholarship from the European Union and an ESMO scholarship. In 2012-2013 she is awarded the annual scholarship “Teodora Zaharieva” for young medical specialists in Bulgaria. She is also awarded the “Favorite Teacher” Award for 2014 from the Faculty of Medicine, English Language Education at the Medical University - Varna. Dr. Assia Konsoulova speaks 4 foreign languages - English, French, Russian and German.



**Dr. Iveta Stoyanova**

Dr. Iveta Stoyanova was born on April 22, 1989 in Plovdiv. She graduated Medicine at the Medical University in Plovdiv. Dr. Stoyanova has worked as a doctor in the Department of Medical Oncology, at MBAL Uni Hospital since September 2016. She has previously worked as a physician at Medline clinic in Plovdiv. Currently, she specializes in Medical Oncology. Dr. Iveta Stoyanova is a member of BMA.

## Dr. Lachezar Vassilev



Dr. Lachezar Vassilev was born on March 22, 1989 in the town of Septemvri. He graduated from the Medical University in Plovdiv. Dr. Vassilev has worked as a doctor in the Department of Medical Oncology, at MBAL Uni Hospital since March 2017. Previously, he has worked with drug addicts in AGPSPP Philippopolis, Plovdiv, and as a doctor in Emergency Medicine, CMSP Plovdiv. He is currently specializing in Medical Oncology.

## Dr. Dimitar Dimitrov



Dr. Dimitar Dimitrov studied at the Medical University of Sofia, where he graduated in 2008 “cum laude”. Upon graduation, he specialized Gastroenterology in UMHAT Tsaritsa Yoanna – ISUL in Sofia. He worked at MHAT St. Ivan Rilski 2003 in Dupnitsa, at Military Medical Academy in Sofia, and since 2016 – at Uni Hospital in Panagyurishte. Dr. Dimitrov is certified in both diagnostic and therapeutic abdominal ultrasonography and gastrointestinal endoscopy. His clinical and scientific interests include interventional procedures in Gastroenterology, progression of chronic liver diseases, hepatocellular cancerogenesis, contemporary treatment of chronic viral hepatitis, and autoimmune liver diseases.

## Dr. Lyubov Simeonova



Dr. Lyubov Simeonova is a doctor at the Clinic of Chemotherapy in SBALO, Sofia. She has graduated secondary education at Goethe School in Bourgas, Bulgaria in 2007. Later on, she graduated Medicine at the Medical Faculty of Sofia Medical University in Sofia in 2014. She has been specializing Medical Oncology at the Clinic



of Chemotherapy at SBALO since 2015.

Dr. Simeonova has attended a number of courses including Innovations in the treatment of colorectal cancer - Zagreb, Croatia (2016), and a training in Medical Law and Genetics in Oncology (2016).

Dr. Simeonova has taken part in various national conferences on Medical Oncology. She is a member of the Bulgarian Oncological Scientific Society, and Young Oncologist Club - Bulgaria. She has also served as a sub-investigator in Phase I and Phase III clinical trials. The scientific interests of Dr. Lyubov Simeonova are in the fields of colorectal and breast cancer.



**Dr. Nedyalka Velikova**

## **Role of Stereotactic Body Radiation Therapy (SBRT) in Oligometastatic Colorectal Cancer: An Opportunity for Cure?**

Improvements in systemic therapy for metastatic colorectal cancer (mCRC) have enabled prolongation of survival. This has subsequently increased the relative significance of local therapy especially for patients with oligometastases.

Colorectal cancer (CRC) is one of the most frequently reported tumor histologies that present oligometastatic spread (synchronous oligometastatic, oligorecurrent or oligoprogressive disease), most commonly in the liver and lung. “Oligometastatic disease” is defined as a state in which metastases are limited in number and site and local therapy could have a potentially curative role. Resection is the standard therapy in most setting of oligometastases. Surgical removal of liver and lung lesions is apparently associated with a better survival (ranging from 37 to 58% at 5 years), even in the absence of controlled randomized data. Recently, technological advances in Radiation Oncology permitted the introduction of Stereotactic Body Radiation Therapy (SBRT) as a non-invasive alternative for achieving local control. SBRT is a novel treatment modality that delivers ablative dose of radiation to the extra-cranial sites with high precision using single or a small number of fractions. Many non-randomized studies have shown that SBRT for various lesions results in good outcomes, both in curative and palliative setting. SBRT was investigated mainly in the treatment of liver and lung metastases with good safety profile, low morbidity and promising results in terms of local control probability with control rates of about 80% and even higher for patients treated with high-dose regimens. The indications of SBRT for other metastatic sites and conditions include isolated lymph nodes, spinal, brain and adrenal metastasis, and post-surgical pelvic recurrence. It is still a potential challenge to select patients with limited metastases who are most likely to benefit from aggressive local treatment and how to combine it with systemic therapies. Based on published studies,

SBRT might have major benefit for a patient with disease free survival more than 12 months, control of the primary tumor, small lesions, limited number of lesions and higher radiation dose delivered.

SBRT appears safe and effective for treating oligometastatic CRC but well-designed collaborative trials are still necessary to draw final conclusions.

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Dr. Nedyalka Velikova has graduated Medical University – Sofia in 2009. She did her training as a resident in Specialized Hospital for Active Treatment in Oncology – Sofia. She acquired specialty in Radiation Oncology in 2014 and continued to work as an assistant professor in the Radiotherapy Department in the same hospital until 2015. Now Dr. Velikova is part of the radiation oncology team working in Acibadem City Clinic Cancer Center – Sofia. During her residency she attended several training courses at ESTRO, IAEA and Prime Oncology in Slovakia, Greece, Slovenia, Spain, Turkey, Hungary, Switzerland and Italy. She has participated in numerous conferences as a speaker and in 2011 won the prize for best performance of the Eight National Congress of Oncology, Boyana Residence, Sofia. In 2014 she won an international scholarship supported by Avon Foundation for Women and became one of the 23 experts from all around the world working in the field of breast cancer selected to study in the US. Dr. Velikova visited the ASCO Annual Meeting in Chicago and spent two months in New York Presbyterian Hospital / Columbia Medical Center, New York working with some of the world-renowned experts in the field of hypofractionated and intraoperative radiotherapy. Dr. Nedyalka Velikova is a member of Bulgarian Guild of Radiotherapy, Bulgarian Association of Radiology, Bulgarian Cancer Society, Bulgarian Association of Medical Oncology, the Young Oncologist Club, the European Society for Radiotherapy and Oncology (ESTRO) and the American Society of Clinical Oncology. Dr. Velikova's main clinical interests are focused on Breast cancer, Gynecological cancer and CNS tumors, Interstitial and Intracavitary HDR Brachytherapy, SRS and SBRT.


## Dr. Tanya Zlatanova



### Metastatic colon cancer – chemotherapy or immunotherapy - challenges and controversies

Colorectal cancer (CRC) remains a significant cause of morbidity and mortality worldwide with high disease incidence. Significant numbers of patients present with advanced, metastatic disease. Over the past 20 years, the therapeutic armamentarium for metastatic disease has increased significantly; 10 new drug approvals include targeted biologics and tyrosine kinase inhibitors. With this increase in options, median overall survival (OS) for patients with metastatic CRC has increased to more than 30 months. With more drug options, and more combination options now available, optimal sequencing of these options to maximize the OS benefit for patients is of great importance.





Despite significant improvements in the management of advanced colorectal cancer (CRC), patients with chemo-refractory disease continue to have poor prognosis, with survival of only around 7 months. This indicates a high unmet need for novel treatment strategies in this patient population.


Immune therapy offers new therapeutic options for patients with chemo-refractory mCRC, and it remains a topic of continued investigation. A lot of questions remain unanswered – the issue of the best biomarker, the most effective combinations/I-O + I-O, I-O+ targeted therapy, I-O +chemotherapy, identifying the best setting to use the drugs/.

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Dr. Tanya Zlatanova graduated Medicine at Sofia Medical University in 2001. Later on, she specialized in Internal Medicine and got her degree in 2008. From 2004 till 2009, Dr. Zlatanova had been working in MBAL Ihtiman. She has also worked as a doctor in Tokuda Hospice in the period 2009-2012. Since March 2012, Dr. Zlatanova has been a member of the team of the Oncology Department at Tokuda Hospital. Dr. Tanya Zlatanovahas quite an experience presenting clinical cases at workshops in Bulgaria and abroad. She has participated in the ESMO Preceptorship on Immuno - Oncology, Siena, Italy(July, 2016), in the NET Diagnostics and Treatment Course, Uppsala, Sweden(November, 2015), in the 2nd ESO-ESMO Masclass on Medical Oncology for Eastern Europe and the Balkan Region in Bratislava, Slovakia (July, 2015), in the Symposium on Immuno - Oncology organized by ESMO in Geneva, Switzerland (November, 2014), and in the ESMO Preceptorship on Immunotherapy of Cancer in Lausanne, Switzerland (March, 2014). Dr. Zlatanova did a specialization in CECOG Targeted Drug Fellowship (September, 2016) at the Department of Oncology, Complex Oncology Center Vienna, Medical University Vienna, Austria. Dr. Tanya Zlatanovagot her Medical Oncology degree at the beginning of 2017. She is a member of ESMO, ASCO, and Young Oncologist Club Bulgaria.

## Dr. Romyana Mitova

Dr. Romyana Mitova has graduated the 114 English Language School in Sofia (1976) and the Medical University in Sofia in 1982. She got her Internal Diseases specialty in 1988 and the one in Gastroenterology in 1990. At the start of her career, Dr. Mitova has worked at the regional hospital in Blagoevgrad for 1 year, before moving to the Clinic of Gastroenterology at the University Hospital Queen Yoanna – ISUL, in which she has worked as a Chief assistant for 30 years. Professional and scientific interests of Dr. Mitova are in the field of gastro-duodenal, pancreatic and hepatobiliary pathology. Dr. Romyana Mitova has 73 scientific journal publications and has attended 49 local and international congresses. She has also participated in 10 different phase II and III clinical trials on duodenal ulcer, hepatic cirrhosis, chronic hepatitis and chronic pancreatitis. Dr. Romyana Mitova is a Secretary and a member of Bulgarian Association of Ultrasound in Medicine, a member of the Board of European Federation of Ultrasound in Medicine, and a member of Bulgarian Society of Gastroenterology.





**Prof. Jasna Mihailovic**



## **PET/CT Diagnostics in Colon Cancer: Challenges and Current Issues**

In the United States, CRC (colorectal cancer) is one of the most common malignancies in humans. It is at third place behind lung and prostate cancer in men and behind breast cancer and lung cancer in women, accounting for 8% of all new cancer cases for both genders. The American Cancer Society estimates 95,520 new cases of colon cancer and 39,910 new cases of rectal cancer in the United States for 2017. F-18 fluorodeoxyglucose positron emission tomography (FDG-PET or FDG-PET/CT) is a new imaging technique that detects malignant (residual/recurrent) tissue according to their increased glucose uptake. However, the FDG-PET has no role in screening, preoperative diagnosis or initial staging in CRC, mainly due to difficulties in distinguishing focal physiologic activity from malignant bowel uptake. During the postoperative follow-up, CT has been shown as not highly accurate for early detection of local recurrence. On another hand, the FDG-PET has significant accuracy in detection of CRC recurrent disease. According to the 3rd German Interdisciplinary Consensus Conference, FDG-PET is graded as 1a indication for relapsing colorectal cancer. In staging the local recurrence, FDG-PET shows better accuracy than CT, with a sensitivity and specificity of 100 and 86%, versus 75% and 100, respectively. Furthermore, the 18F-FDG PET/CT improves staging accuracy in colorectal cancer from 78% to 89%, if compared to FDG-PET alone. Additionally, FDG-PET has higher accuracy in detecting hepatic and extrahepatic metastases in comparison to CT and CT portography (92% versus 78% and 80%) in contrast to higher sensitivity of CT portography. FDG-PET also shows excellent sensitivity in detection of local recurrence after radiation therapy. It was reported that PET is more accurate (90%-100%) than CT (48%-65%) in distinguishing post-therapy scar from recurrent disease. Serum carcinoembryonic antigen (CEA) is a well established tumor marker in detection of local tumor recurrence and metastases in the postoperative surveillance in patients with CRC. Increasing CEA during the follow-up might be an important indicator of CRC recurrent disease. According to the results of some authors, 18F-FDG PET/CT has sensitivity of 93% and specificity of 74% for detection of recurrence and/or metastasis in patients with elevated serum CEA. In another study, in CRC patients with elevated CEA levels and negative CT scan, FDG-PET correctly detected recurrence in more than 30%. Conclusion: 18F-FDG PET/CT has a great value in the management of the patient with colon cancer. Although not specifically relevant in screening of the initial diagnosis, it has a role in preoperative evaluation of apparently limited metastatic disease, detection of recurrent disease, clarification of equivocal lesions at initial staging and evaluation of unexplained rising tumor markers. FDG PET/CT is also useful to assess the efficacy of therapy although the criteria are different for different gastrointestinal tumors. These criteria are still being developed. Finally, nuclear medicine physicians and radiologists need to be alert to the incidental identification of foci in the gastrointestinal tract that may represent neoplasm when performing whole body FDG PET/CT for other reasons.


*Key words: F-18 fluorodeoxyglucose, Positron-Emission Tomography; Colon Cancer; Staging; Follow-Up*

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Professor Jasna Mihailovic is the Head of Department of Nuclear Medicine at the Oncology Institute of Vojvodina, Serbia. She is also Full Professor at Department of Radiology, Medical School, University of Novi Sad and President of Serbian Society of Nuclear Medicine since October 2016.

She trained in Nuclear Medicine and sub-specialised in Oncology; obtained her MSc and PhD degree from the University of Novi Sad in Imaging of thyroid nodules.





Previous to this Professor Mihailovic had several international fellowships, namely in Medizinische Hochschule Hannover, Berlin, Klinikum Steglitz, Berlin, Hospital I Provincial de Barcelona, Barcelona, Spain, FU Berlin, Klinikum Steglitz, Berlin, Royal Melbourne Hospital in Melbourne, Australia, Centre Leon Berard in Lyon, France, Nuklearmedizinische Klinik, TU-Muenchen, Germany Klinik für Nuklearmedizin der Universität Bonn, Germany, Klinik und Poliklinik für Nuklearmedizin, Ludwig-Maximilians-Universität, Klinikum Grosshadern, München and Cornell University, New York Presbyterian Hospital, Division of nuclear medicine, New York, New York, US.

Prof Mihailovic is a member of the Thyroid Committee of European Association of Nuclear Medicine, in charge for education and also SNMMI member. She has delivered numerous invited talks, presented research papers at national & international meetings, organised multiple international and national nuclear medicine meetings as either President of Organising Committee or member of Scientific committees. Prof Mihailovic has publications in reputed peer-reviewed journals and written several book chapters. Professor Mihailovic is a member of the Editorial board and reviewer for journals, including EJNMMI, NMC, Annals of Thyroid Imaging, International Journal of Radiology and European Journal of Endocrinology. Her sub-specialist subjects are thyroid imaging, PET-CT and cancer imaging.


## Dr. Jordan Genov

Dr. Jordan Genov has graduated the Medical University in Sofia in 1991 and got his Internal Diseases specialty in 1998 and the one in Gastroenterology in 2005. He also acquired a PhD degree in 2008. Meanwhile, Dr. Genov carried out 2 specializations - in Gastroenterology, at the Dutch Association of Hepatogastroenterology, The Netherlands (1995) and in Hepatology at the University Hospital Paul Brusse, Paris, France (2010).

Dr. Genov has worked at the hospital in Kostenec at the beginning of his career, after which he has dedicated more than 20 years to the Clinic of Gastroenterology at the University Hospital Tsaritsa Yoanna – ISUL, where he first worked as an assistant professor (1994), and then as an associate professor (2010). Since 2010, Dr. Genov is the Head of the Department of Hepatology in the mentioned Clinic of Gastroenterology.

Professional and scientific interests of Dr. Genov are in the field of chronic viral hepatitis, liver tumors, liver diseases and liver transplantation, management of portal hypertension, intrahepatic cholestasis, US-guided interventional procedures, chronic and acute pancreatitis, and pancreatic tumors. Dr. Jordan Genov has 147 scientific publications and has attended 94 local and international congresses.

Dr. Jordan Genov is a Member of the Board of Directors of Bulgarian Society of Gastroenterology, a Secretary of Bulgarian Association for The Study of The Liver, a Chief of the Advisory Board of Bulgarian Association for Ultrasound in Medicine. He is also a member of European Association for Study of the Liver (EASL), the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB), the Australoasian Society for Ultrasound in Medicine (ASUM), as well as a Member of Local Ethical Commission in University Hospital Tsaritsa Yoanna - ISUL.





## Sanofi Genzyme Symposium: Biomarker data utility in tailoring treatment decisions in mCRC

### Plasma and tissue biomarkers in mCRC: retrospective analyses of the VELOUR trial

There are several anti-VEGF and anti-EGFR agents approved for 2<sup>nd</sup> line treatment of patients with metastatic colorectal cancer (mCRC) in combination with different chemotherapy backbones. Although these agents are included in the ESMO and Bulgarian recommendations for mCRC treatment <sup>1,2</sup>, the factors predicting the response of each individual patient to these therapies have not been completely elucidated. In the last years, different biological biomarkers have emerged as some of the most promising prognostic and predictive variables for a wide range of malignancies, including mCRC.

Such biomarkers can be detected in the tumor microenvironment and are associated with different resistance mechanisms after first-line treatments for mCRC<sup>3</sup>. The presented plasma biomarker data has been collected as part of a retrospective study<sup>4</sup>, conducted with samples collected from 553 patients who participated in the VELOUR trial<sup>5</sup>. The observed effect of previous anti-angiogenic treatment on the plasma levels of multiple pro-angiogenic factors, including PlGF and VEGF-A are discussed. Results from a non-interventional investigator sponsored study on tissue biomarkers in mCRC are also presented. This research examined the effect of KRAS, RAS, BRAF and sidedness status of the patient's tumor on the response to aflibercept treatment<sup>6</sup>.

This lecture aims to reinforce the oncologists' knowledge of how biomarker data can support 2<sup>nd</sup> line treatment decisions for mCRC patients.

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Dr Ivan Tonev is a nationally recognized medical oncologist, currently working as Head of the Department of Medical Oncology (MO) and Oncology diseases in Pneumology in Complex Oncology Center, Plovdiv. He graduated Medicine from MU Varna in 2001 and obtained specialty in internal Medicine in 2009 and then a second specialty in MO in 2014. He worked in the MO Department of UMBAL "Sv. Marina" and as an Assistant in the Medical University in Varna from 2003 to 2014, before joining his current team in Plovdiv.

#### mCRC Clinical case 1

Dr Milena Kyoseva graduated Medicine from MU Plovdiv in 2005 and obtained specialty Medical Oncology in 2014. She worked in the MO Department of UMBAL "Sv. Georgi" in Plovdiv from 2008 to 2016 before transferring to her current job in the MO Department in MBAL "Park Hospital" in Plovdiv.

#### mCRC Clinical case 2

Dr Eliz Tazimova graduated Medicine in MU Sofia in 2013 and currently specializes Medical Oncology at MBAL "Tokuda" in Sofia. Her professional interests include targeted therapy and personalized medicine in oncology.



## Dr. Snezhina Nedeva

Dr. Snezhina Nedeva was born on August 12, 1987 in the town of Plovdiv. She graduated Medicine at the Medical University in Plovdiv in 2012. Since November 2013, Dr. Nedeva has worked as a doctor in Central OncoHospital Plovdiv, Bulgaria. She has had numerous trainings and courses in Medical Oncology and has attended a number of conferences and congresses both in Bulgaria and abroad.

Dr. Snezhina Nedeva is a member of BMA and speaks two foreign languages – English and German.

## Dr. Plamen Getsov

Dr. Plamen Getsov is a consultant radiologist at Spectar Diagnostic Imaging Centre in Sofia, Bulgaria.

Dr. Getsov graduated the Medical University in Plevna in year 2000 and 6 years later he got his specialty in Radiology at Sofia Medical University. He has worked as a full-time radiologist in the Department of Diagnostic Imaging at Hristo Botev Hospital in Vratsa, and later on as a radiologist in the Diagnostic Imaging Clinic at Queen Joanna University Hospital in Sofia. Since 2007, Dr. Getsov has holds a teaching position of an Assistant Professor in Radiology, in the Faculty of Medicine at St. Kliment Ohridsky University in Sofia.

Dr. Getsov has more than 50 different publications in the field of MRI, CT and ERCP.



## Dr. Jossif Assa

After graduation as a Physician in 1993 at Medical University Sofia, Dr Jossif Assa has worked for in Bayer, Smith Kline Beecham and merged GSK as a medical representative and Sales Manager.

In march 2002 he joined a team of Janssen-Cilag as a Product Manager for Gastroenterology, Neurology and Psychiatry. Since 2013 as Marketing Manager is responsible for the oncology portfolio in Intellect Pharma Plc, a partner of Janssen, Pharmaceutical companies of Johnson & Johnson for Bulgaria.



**Prof. Sonya Sergieva**



## **Nuclear Medicine Approaches in Prostate Cancer – Challenges and Controversies**

There is a limited role of nuclear medicine in imaging of primary prostate cancer – bone scan is the only method used for staging of disease in cases with high PSA levels. Baseline whole body scan followed by SPECT-CT imaging is an advanced diagnostic technique for diagnosis, staging and follow-up of patients with bone metastases. Radionuclide imaging is applicable mainly in patients with biochemical progression and suspicious of prostate cancer recurrence. SPECT-CT Indium  $^{111}\text{In}$ -capromab pendetide (ProstaScint®), is a radiolabeled monoclonal antibody to prostate-specific membrane antigen, which offers a potential means of localizing sites of bone and soft tissue metastasis in studied patients. PET-CT and PETMRI with  $^{11}\text{C}$  choline/ $^{18}\text{F}$  fluorocholine have clinical role for visualization of tumour cells located in prostate bed, lymph nodes or distant organs. Choline is an essential component of phospholipids in the cell membrane. Increase in cell proliferation and the enzyme activity is associated with an increase in choline uptake.  $^{68}\text{Ga}$ -PSMA PET/CT or PET/MRI is able to show pathological accumulation outside the prostate bed in PSA levels as low as  $< 0.5$  ng/ml. Both primary and metastatic prostate carcinomas show rapid uptake of  $^{68}\text{Ga}$  PSMA, used for correct biopsy of the primary tumor, exact N/M staging and restaging of the disease.  $^{68}\text{Ga}$ -PSMA PET/CT or PET/MRI can detect the glandular relapses and metastases with significantly improved contrast when compared to choline-based PET/CT, especially at low PSA levels. This novel technology is the basis for prediction of individual therapeutic response with  $^{177}\text{Lu}$ -PSMA treatment, components of the promising theranostic approach in prostate cancer.

*Key words: Prostate Cancer, SPECT/CT, PET/CT, PET/MRI, Choline,  $^{68}\text{Ga}$ -PSMA*

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Prof. Sonya Borisova Sergieva is a nuclear medicine specialist who works in Sofia City Oncology Dispensary and as of 2013 is an Associate Professor at the Specialized Hospital for Treating Oncology Diseases in Sofia.

Dr. Sergieva graduated the Medical Academy in Sofia in 1990 and specialized Nuclear Medicine in the National Oncology Center and Alexandrovska Hospital in Sofia in the period 1991-1994. After getting her nuclear medicine diploma in 1994, she moved on specializing in oncology and finished her second specialization in 1998.

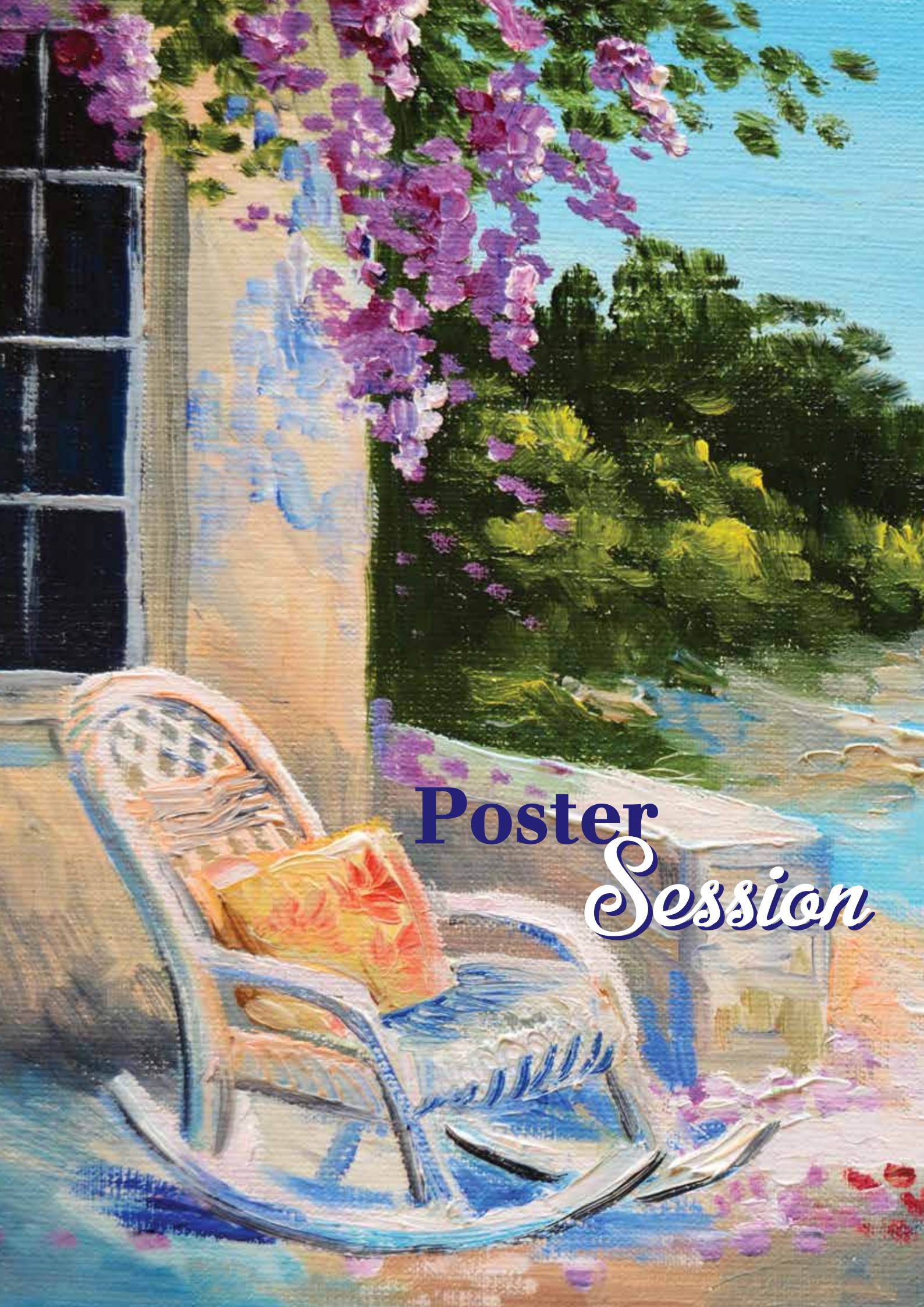
Dr. Sonya Sergieva started her career in the National Oncology Centre in Sofia where she worked from 1991 till 2002. Later on, she moved to the Department of Nuclear Medicine in Sofia City Oncology Dispensary, which she headed for 10 years from 2003 till 2012.

Prof. Sergieva has a lot of experience in the field of clinical trials being a coinvestigator, and has participated in 8 scientific projects, half of them international. She is currently a member of Bulgarian Association of Nuclear Medicine, Bulgarian Scientific Oncology Society, the European Association of Nuclear Medicine (EANM) and BUON.

Dr. Sergieva has 84 publications in both Bulgarian and international scientific magazines and is an author of more than 130 reports and resumes delivered at local and international scientific events. Her dissertation topic is about the diagnosis and differential diagnosis of malignant melanoma using radio-marked monoclonal antibodies.

Prof. Sonya Sergieva speaks Russian and English as foreign languages.





Poster  
*Session*



## Clinical application of SPECT-CT with $^{99m}\text{Tc}$ -Tektrotyd in patients with neuroendocrine tumors (NETs)

**S. Sergieva MD, A. Saint Georges MD, A. Fakirova MD, B. Robev MD**

Functional imaging procedures applying various gamma-emitted radiopharmaceuticals are used for staging, assessment of SSTR status and making decision on the optimal treatment plan in patients with NETs. The latest development in the imaging of NETs is the fusion of anatomical and functional modalities.

**Purpose:** The aim of this study was to investigate clinical application of somatostatin SPECT-CT studies with  $^{99m}\text{Tc}$ -Tektrotyd in patients with NETs.

**Material and Methods:** 89 patients with various NETs were studied: 41 with GEP NETs; 17 with mediastinal and pulmonary carcinoids; 11 with MTC; 5 with lymphomas; 3 with breast NETs; 2 with prostatic NETs; 2 with ovary NETs and 1 with epiglottal NET.

155 examinations including SPECT-CT studies of the neck and chest and/or abdomen were performed 2-4 hrs post i.v.inj. of 555-740 MBq  $^{99m}\text{Tc}$ -HYNIC-TOC (Tektrotyd, Polatom), using SPECT-CT gamma camera Symbia T2, Siemens. Patients were studied after 4 weeks of withdrawal Sandostatin LAR if applicable and emptying GIST before SRS. Functional imaging were compared to biochemical evaluation of tumors that secrete markers: CgA/Calcitonin respectively. Our results were interpreted based on all other clinical and radiological data.

**Results:** In 4 out of 8 pts with UPO, primary tumors were established – MTC and mesenteric NET proven after biopsy and surgery. Therapy effect was determined in the other 4 pts but because of the advanced metastatic process primary tumor was not possible to differentiate. Exact N/M-staging was performed in 38 pts: loco-regional lymphadenopathy, distant liver and/or pulmonary metastatic lesions overexpressed somatostatin receptors were imaged in 28 of them. In 6 cases tracer uptake was very low significant for insufficient receptor expression. Four patients were true negative for secondary lesions.

In the rest 36 pts SPECT-CT studies were used to evaluate effect of complex therapy:

- Complete therapeutic response was obtained in 3 pts.
- Partial response – in 12 pts.
- Stable disease – in 9 pts.
- Progressive disease – in 12 pts. In 4 pts the presence of a malignant tumor was not corroborated by biochemical findings – level of CgA was  $< 100$  ng/ml.

High tracer uptake was obtained in 6 benign tumors – in 2 suprarenal adenomas; in 3 thyroid adenoma and in 1 benign ovary cyst. Intensive physiological uptake was shown in the both breasts of 2 young women ( $< 35$ yo) due to fibrocystic alteration and in 1 pt with accessory spleen.

SPECT-CT with  $^{99m}\text{Tc}$ -Tektrotyd is a potential new tool for staging and follow-up of patients with NETs in the coming years.



## Radiation exposure to patients and medical staff in different procedures of nuclear medicine

**M. Dimcheva MD, A. Jovanovska MD,**  
**Sofia Cancer Center, Department of Nuclear Medicine, Sofia BULGARIA**

The aim of this study is to provide information on developing technologies and clinical techniques for hybrid SPECT/CT imaging using ionizing radiation and their associated radiation dose to patients and medical staff. A thermoluminescent dosimeters (TLD) was used in this study to analyze the historic records of the external radiation doses to staff members working in our nuclear medicine department in 7 procedures, including elution of  $^{99m}\text{Tc}$  from  $^{99m}\text{Mo}/^{99m}\text{Tc}$  generators, syringe preparation, radiopharmacy kit preparation, injection, accompanying patients, SPECT/CT scan, oral  $^{131}\text{I}$  preparation. These dosimeters was worn by the staff members at the level of the chest on the front part of the body. A retrospective review of 100 clinical studies of various nuclear medicine procedures ( $^{99m}\text{Tc}$ -MIBI-Tetrofosmin,  $^{99m}\text{Tc}$ -MDP bone scan,  $^{99m}\text{Tc}$ -Tektrotyd,  $^{99m}\text{Tc}$ -Thyroid imaging,  $^{99m}\text{Tc}$ -Nanocoll,  $^{131}\text{I}$ -Nal(diagnostic application 185MBq) obtained on hybrid SPECT/CT systems was performed to calculate the effective radiation dose to patients. The results from this study showed that annual effective radiation doses to nuclear medicine department staff members were within permissible levels. The contribution of total effective radiation dose from SPECT component were calculated using the activity of the injected radiopharmaceutical and dose tables published by the conversion factors listed in ICRP 53 and ICRP 80. The radiation dose for CT was calculated by Dose Length Product method. According to the results of this study the dose in each procedure depends on different factors such as the education and experience of the staff members, usage of shielding and taking the radiation protection requirements into consideration. When SPECT-CT is being performed, all measures should be taken to reduce both the radiopharmaceutical dose and the CT effective dose following the ALARA principle.

## Sorafenib/Nexavar – Treatment Headway for Metastatic Thyroid Cancer

**I. Stoyanova MD, R. Krasteva MD, L. Vassilev MD**

**OBJECTIVE** Reviewing the treatment efficacy of Sorafenib/Nexavar (a kinase inhibitor drug) for metastatic thyroid cancer, presented in a case study, showing a potential treatment headway.

**METHOD** The evaluation of Sorafenib/Nexavar is supported by data, gathered through a detailed clinical case study, supported by medical imaging, which presents a 63 year old woman initially diagnosed in 2015 with no data for family history.

**RESULTS** After approximately one year of treatment, the use of Sorafenib/Nexavar has been tolerated very well by the patient. The imaging results show a stable disease, even a reduction in the size of pathological images. The quality of life both observed by the clinicians and shared by the patient has demonstrated improvement.

**CONCLUSIONS** The results show that while metastatic thyroid cancer is still a challenge for clinicians of various



fields, Sorafenib/Nexavar, being the only proven target agent to impact late diagnosed thyroid cancer, is suggesting a positive prognosis. More in-depth research of the efficacy of the drug offers hope for patients in the future.

*Key words: thyroid cancer, Sorafenib, Nexavar, quality of life, target therapy*

## Clinical Experience with Stereotactic Body Radiation Therapy in Patients with Liver Metastases at MHAT “Uni Hospital”

**N. Tolev MD**

**Purpose:** A new alternative therapeutic option for liver metastases is Stereotactic Body Radiation Therapy (SBRT). This is a method of external beam irradiation, which accurately delivers a high dose of radiation in one or a few fractions of an extracranial target. The primary endpoint is in-field local control. As secondary endpoints are considered the monitoring of metastases evolution and control over the hepatic toxicity.

**METHOD:** A prospective study was started in our department in May, 2017. We treated 6 oligometastatic patients, 4 men and 2 women with a median age of 60 years, diagnosed with different primary tumors and histology. The number of lesions was 7, with maximum individual tumor diameters of less than 6.6 cm. Three of the patients had previous local treatment. One had resection surgery and Radiofrequency ablation (RFA), one had only RFA and one had RFA and alcohol ablation for two liver metastases. The patients received dose escalation (16-22Gy/1 fraction to 28.5-30Gy/3 fraction) and one was simultaneously treated for paraaortal lymph nodes metastases with 16Gy/1fr. The assessment of tumor response was conducted through EORTC-RECIST and PERCIST criteria. Toxicity was classified according to the Common Toxicity Criteria, version 3.0.

**Results:** In-field progression was observed in 2 lesions. According to PERCIST criteria at 6 months after SBRT, CMR was observed in 1 patient; PR in 1 patient; PD in 1 patient with new liver metastases and a progression of other metastases. One patient had reduction in SUV at 3 months and reduction of the lesion on MRI at 4 months. One patient had PD on CT scan at 4 months with new hepatic metastases and a progression of other metastases. The last patient had volume reduction and necrosis within the irradiated lesion at 3 months. No patients have experienced a radiation-induced liver disease or grade  $\geq 3$  toxicity.

**Conclusion:** Local control in this minor cohort can't be reliably measured. There is a tendency in the progression of the disease, stating that, after radiosurgery, these dosing regimens are not sufficient enough to ablate existing and treated metastases. The doses in patients with a stable disease are enough for full local control. Dosing regimens should be individualized and higher than these used in this study.



# Clinical Use of Zytiga and Xtandi in the Treatment of Metastatic Prostate Cancer Reviewed through Three Case Studies

**L. Vasilev MD, R. Krasteva MD, I. Stoyanova MD**

**OBJECTIVE** Evaluating the effect of treatment with Zytiga (a selective, irreversible inhibitor of cytochrome P17) and Xtandi (enzalutamide) in three patients with metastatic prostate cancer.

**METHOD** Three case studies of men diagnosed with prostate cancer were used to gather the necessary data and analyze the effect of the treatment. Of them, one is being treated with Zytiga, two are being given Xtandi. The cases are being closely followed and supported by medical imaging in order to gain clinical evidence on the efficiency of the treatment and the ways it has impacted the patients' quality of life.

**RESULTS** The information provided by the followed cases affirms the good therapeutic response of the given agents, managing a stable disease, and their suitability for application as a second line hormonal therapy for patients with metastatic prostate cancer. The medical quality of life of the followed patients does not show decline.

**CONCLUSIONS** The evaluation results provide grounds to continue the application of Zytiga and Xtandi as a second line hormonal treatment of metastatic prostate cancer both due to the good clinical effects and the stable indicators of the quality of life. The presented cases are being continually followed by clinicians in order to obtain a more thorough understanding of the agents in question.

*Key words: prostate cancer; Zytiga, Xtandi, quality of life, hormonal treatment*



## Dr. Samuil Katov



Dr. Samuil Katov graduated the foreign language high school of Pleven (2011) and the Medical University in Sofia in 2018. As of February 2018, he works as a graduate in medical oncology of Medical Oncology at Queen Joanna University Multiprofile Hospital for Active Treatment in Sofia, Bulgaria.

During his studies at the university, Dr. Katov has had a number of internships in the juvenile surgery units (in Georgi Stranski University Hospital in Pleven), in the cardiology and pulmonology clinic, in an intensive care unit, and in the unit of hepato-biliary and pancreatic surgery in Alexandrovska University Hospital in Sofia.

Dr. Katov has also 2 years of experience working for IMS as an interviewer in marketing researches regarding new medical products.

Dr. Samuil Katov speaks two foreign languages - English, and German.

## Dr. Hristo Spassov



Dr. Hristo Spassov is an intern, working and specializing in medical oncology since 2014 at Serdika Hospital in Sofia, Bulgaria.

Dr. Spassov has graduated Plovdiv English Language School in 2007 and Sofia Medical University in 2014. During his medical education he has participated in European Youth exchange programmes in Czechia and Poland.

Dr. Spassov speaks 2 foreign languages - English and German.





**Dr. Mauro Papotti**

## **Personalized Therapy: How to Test Cost-effectively and Evidence-based for Predictive Markers**

A cost-effective test of predictive markers in lung cancer requires their preliminary accurate classification, which is usually obtained by conventional staining and a minimal panel of phenotypic markers in the case of poorly differentiated tumors or poorly cellular cytology/biopsy specimens. These include p40 for squamous carcinoma, TTF1 for adenocarcinoma (ADC) and chromogranin or synaptophysin for neuroendocrine neoplasm. Spared tissue is fundamental for subsequent testing of predictive markers. These can be analyzed in any sample, either biopsy or cytology, provided adequate cellularity or tissue preservation is present. Ideally, analytic methods best detect mutations in samples having >20% malignant cell content. The new 2018 recommendations from IASLC/CAP indicate three gene categories for investigation, currently established for advanced ADC only: 1- “must-test” (EGFR, ALK, ROS1, which are standard of care); 2- “should-test” (an expanded gene panel includes BRAF, MET, RET, HER2, and probably KRAS); 3- the remaining are considered investigational biomarkers, not appropriate for clinical use at this time. As for methods, mutational analysis is the standard in most centers, while IHC was accepted as a FISH alternative to detect ALK rearrangements, but not to replace EGFR mutation detection. In relapsing diseases, analysis of EGFR 790 mutation (but not of ALK mutations) is recommended, better on re-biopsy material than on circulating free DNA. No specific recommendations exist for non-ADC neoplasms. In the future, other markers, such as ROS1, might be tested by IHC or by alternative procedures (e.g. Nanostring technology). Regarding NGS, no specific recommendations were currently provided due to insufficient data, although the evaluation of large gene panels has the obvious advantage of providing numerous information at a time, provided an accurate data interpretation is associated. Regarding timing of molecular investigations, some IHC tests can be programmed at the time of diagnostic marker determination, or shortly thereafter. At this step, ALK and ROS1 can be analyzed together with another relevant predictive marker, i.e. PDL1. This can be usefully incorporated in the biomarker list, based on the approval of immune checkpoint inhibitors for lung cancers expressing PDL1 in >50% tumor cells, as defined by specific IHC protocols.

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Present position: Full Professor of Pathology, University of Turin; Head, Division of Pathology, Città della Salute Hospital, Turin, Italy; Vice-Chair, Medical School, University of Turin

Resident program training in Oncology (University of Modena, 1983) and in Pathology (University of Torino, 1991).

**DIAGNOSTIC ACTIVITY** – Since 1982, diagnostic cytology exfoliative and fine needle aspiration biopsies and of pulmonary, thoracic and endocrine surgical pathology. Application of immunohistochemistry and molecular techniques to histological and cytological specimens for diagnostic, prognostic and predictive purposes.

**Teaching activity** - Pathology courses at the University of Turin First Medical School in Turin (years 1992-2003 and from 2015-date) and Second Medical School in Orbassano (from 1997-date). Pathology course at the Laboratory Technician School, University of Turin (1994-date). Cytopathology and surgical pathology courses at the Post-graduate Schools in Pathology, Oncology, Respiratory Medicine, Thoracic Surgery and Endocrinology (years 1987-date).

SCIENTIFIC ACTIVITY – Thoracic pathology (lung and mesothelium), Endocrine pathology (parathyroid, thyroid and adrenal glands as well as neuroendocrine tumors) and immuno-histochemical and molecular biology techniques applied to diagnostic pathology and aspiration biopsy cytology. Receptor analysis in endocrine tumors.

Over 400 papers in peer review journals e 420 abstracts.

Member of the International Academy of Pathology (IAP), European Society of Pathology (ESP), Società Italiana di Anatomia Patologica (SIAPEC), Endocrine Pathology Society, International Association for the Study of Lung Cancer (IASLC), European Neuroendocrine Tumor Society (ENETS).

Since 1982 obtained grants for research projects funded by the National Research Council (Rome), the Italian Ministry of University and Education, the Regione Piemonte (Turin), Fondazione Berlucci, Compagnia di San Paolo (Turin) and the Associazione italiana per la ricerca sul cancro (AIRC, Milan).

Member of the Editorial Board of Pathologica, Virchows Archives, Archives of Pathology, J Endocrinological Investigations, American Journal of Clinical Pathology, Journal of Pathology, J Clinical Pathology.

1990-1999 Secretary and 2000- 2003 President of the “European School of Pathology (ESCoP)”, founded in Torino by the European Society of Pathology (ESP).

## Prof. Lothar Pilz



### Basics in Clinical Statistics

INTRODUCTION: In moving to the principle of evidence based medicine especially for the efficacy in diagnosis and interventional treatment in the middle of the last century, the epoch of clinical trials started and with this, statistical standards are now part of the conditions in methodological and systematic scientific approach in treating patients and improve care. Following this principle, evidence based medicine relies on data sampled in strongly defined populations showing explicit characteristics of certain diseases and of healthy controls, or controls not showing these characteristics. This approach is turning away from patient centered research focusing on single or small groups of patients and will in so far enhance the experience of clinicians. That does not mean that only prospective studies are in the focus, also a systematic retrospective look back is of importance in gaining information. In this talk I will concentrate on the question what the main statistical input is.[1-3]

One aim of evidence based medicine is to demonstrate the activity and efficacy of a treatment or the practicability of a diagnostic method obeying strong criteria (in- and exclusion) for a so defined population. Thus, interpreting medical data means to find an answer to the following questions:

- (i) Which hypotheses support the main aim? How they are related to a real biomedical basis?
- (ii) Which tests are performed under a given level of significance (p-values) to prove the main hypotheses?



(iii) In which tables, graphs, and figures are the research results made visible? What is the information transported by them?

(iv) Are possible associations assessed and quantified by reported measures like p-values and by using confidence intervals to express the uncertainty of those associations?

(v) To state associations, are comparisons made as an inherent part of a statistical analysis?

Some often used statistical methods

1. In hypothesis testing a medical question will be abstractly formulated into a statement. Explicitly it should be a dichotomous decidable question which is appropriate or not, called a null hypothesis. At the same time there is an alternative hypothesis, ideally the negation of the null hypothesis, such that it could be decided by a test if the null or the alternative hypothesis is true. [4]

2. In general the p value stands for the probability to get a result which is equal or even more elaborated, depending on the kind of variable, when the observed result presuming the null hypothesis of no effect is true. Then the probability represents a measure of the magnitude for evidence against the null hypothesis and the theory of hypothesis testing allows for a given effect to reject a null hypothesis in favor of an alternative hypothesis. Fact is that the p value contains no information about the strength of an effect.

3. By convention levels of Type I error ( $\alpha$ ) for rejecting the null hypothesis (if it is true) and Type II error ( $\beta$ ) for accepting the null hypothesis (if it is false) are predefined as well as some critical region or interval. If the test statistics lies in this interval the null hypothesis is rejected in favor of the alternative hypothesis.

4. The level of significance ( $\alpha$ ) is set in advance and part of the analysis plan. Often used levels are 0.05; 0.025; 0.01; and 0.001 which depends on the underlying medical question.

5. Confidence intervals (CI) are used to give some information about the direction or size of a difference or a relative risk between different groups in a result. The p-value cannot give this information. The CI contains values which includes the desired true parameter. Usually a level of 95% is chosen with the meaning that the true parameter will be found in 95 of 100 (repeated) experiments. Important to state is that if sample size and the dispersion of data or a point estimate are known, p values can be transformed into confidence intervals and vice versa. Thus provided enough information the two statistical tools are equivalent.

6. The statistical test procedure calculates the probability to get the observed data (or even 'better' data) under the assumption that the null hypothesis is correct, resulting in a p value from 0 to 1. A small p value indicates a marginal probability for seeing the observed data. The null hypothesis will be rejected if the p value is less than the before predefined level of significance. A typical null hypothesis is that there is no difference in the outcome in two experiments; hence, the difference effect is assumed to be zero.

7. Tables of aggregated baseline data and outcome events are part of most medical journal papers concerning treatments. Often in a table the patients' characteristics is displayed including some demographic variables. The main outcome events are forming the key table of every paper stratified by treatment groups. [5,6]

8. Categorical variables are shown as number and percent by group.

9. Continuous variables can either be presented by mean and the standard deviation or by median and the interquartile range.

10. The Kaplan-Meier plot is the most often used graph to show time-to-event outcomes as death, time to progression, disease free interval etc. In general, a graph displays the steadily increasing difference in incidence rates of the outcome for treatment arms. To make the process clearer, the numbers at risk in each group can be shown at regular time intervals in the time axis. Individuals who did not reach the endpoint are censored (e.g. still alive, lost to follow-up) and should

be marked in the plot. [7]

11. Estimation of treatment effects is to measure the magnitude of the difference between treatments on patient outcomes. Normally this is done by a point estimate showing the actual difference observed. Namely, there are three main types of outcomes: (a) Binary (dichotomous) response; (b) Time to event outcome most measured in intervals; (c) Quantitative outcome as the reduction of a certain percentage of tumor loads at a given time point. [8]

12. Estimates based in percentage are indicated if a binary outcome has to be judged in terms of absence or presence. A confidence interval of the proportion of interest can be given.

13. Estimates for time-to-event outcomes are used in all survival statistics as the Kaplan-Meier estimate is only a time point estimate. Instead, the most common approach is to use a Cox proportional hazards model to obtain a hazard ratio and its 95% confidence interval. [9]

14. Randomization is a process in which each of the patients has the same but not necessarily the equal chance to be assigned to predefined treatment arms ensuring that the treatment arms are comparable with respect to known or unknown risk factors. Used to remove selection and accidental bias and to guarantee the validity of statistical tests.

15. Main design issues of clinical studies are the formulation of the primary aim, the question of blinding, and the boundary conditions of sample size calculations. [10-12]

Examples from medical trials will be used to explain the statistical principles.

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Study of Mathematics and Physics 1973 –1978 at the Johann-Wolfgang-von-Goethe-University, Frankfurt and Eidgenössische Technische Hochschule (ETH), Zürich, Switzerland;

1979-1980 Research Assistant, University of Heidelberg, Heidelberg

1981- 2011 Senior Researcher and Consulting Statistician, Department Mathematical Models / Biostatistics, German Cancer Research Center, Heidelberg


Since 2011 Senior Consultant for Statistics, Medical Faculty Mannheim, University of Heidelberg, Mannheim


Since 2013 Appointed Statistical Consultant, Medical University Bialystok, Poland

**Prof. George Zografos**

## **Challenges and Controversies in Breast Conserving Surgery**

The goals of breast conserving therapy are to provide the low rate of recurrence and survival equivalent of mastectomy, simultaneous staging of the axilla, and a cosmetically acceptable breast. Various prospective randomized clinical trials, directly comparing breast conserving surgery with mastectomy, have shown equivalent survival between the two treatment approaches. Although breast conserving surgery provides an acceptable alternative to mastectomy for the treatment of invasive breast cancer, it is not applicable to all patients. Mastectomy is mandatory for tumor control for some subgroups of patients with breast cancer with specific characteristics e.g. large tumors, multifocal lesions, scattered micro calcifications, etc. Microscopic resection margins are the major selection factor for breast conserving therapy, because of their marked influence on local recurrence. No ink on margin for invasive cancer and 2 mm margins for DCIS are the currently suggested cut offs for margins. MRI can be utilized in order to assess the extent of the disease in the breast and guide further treatment. However, surgical decisions should not be based on MRI findings alone. MRI findings alone should not be used to change surgical planning and conversion from breast conservation to mastectomy. All suspicious findings on MRI require pathologic confirmation. Evaluation of the axilla provides information for treatment decisions in patients with invasive breast cancer. Sentinel node biopsy is the standard initial approach for patients with a clinically negative axillary examination, and the recent ACOSOG Z0011 randomized trial among patients with sentinel node positive breast cancer treated with breast conserving therapy, concluded that axillary lymph node dissection can be omitted in patients with limited involved nodes.





To achieve an acceptable cosmetic result following breast conserving surgery, the application of oncoplastic techniques may be necessary. The goal of the oncoplastic surgery is to remove the portion of the breast containing the cancer and then reshape the patient's remaining breast tissue into a normal-appearing breast. This should always be done without compromising the oncological treatment of the patient.

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Prof. George Zografos is a Professor in Surgery, Director of the 1st Propaedeutic Department of Surgery, Hippocratio General Hospital, Medical School, University of Athens, Greece, and as of 2014 - a Vice Dean of the University of Athens, Athens, Greece.

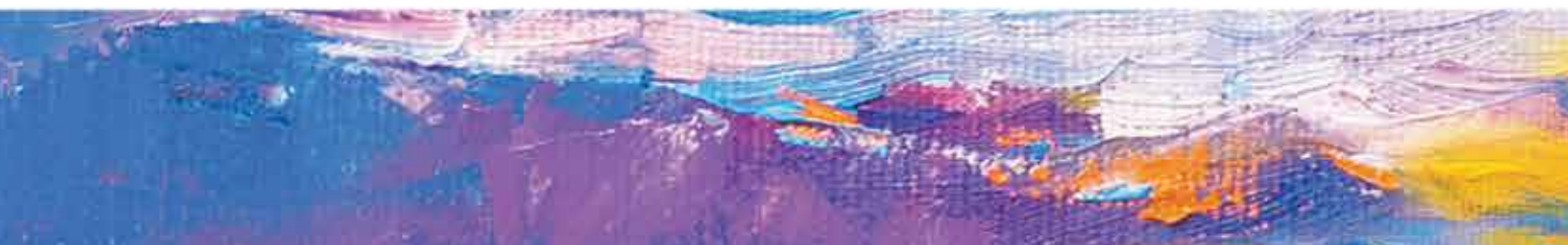
Prof. Zografos graduated the High School of Plaka, Athens, Greece in 1974, and later the Medical School of University of Athens in 1980. Upon completion of military service (1983), he started a specialty and got a title in General Surgery (1986). In 1988, Prof. Zografos got his PhD in Medicine from the University of Athens with a dissertation - Radioisotope angiography with  $^{99m}\text{TcO}_4\text{Na}$  in the study of vascular diseases.

He has enormous clinical experience as a Resident in General Surgery in the period 1982-1990. Prof. Zografos has won numerous fellowships - Registrar & Honorary Registrar in Queen's Medical Centre, Nottingham, UK and Royal Postgraduate Medical School-Hammersmith Hospital, London UK (1988-1990); Surgical Oncology Unit, Roswell Park Memorial Institute Buffalo, New York, USA (1991); GI Surgery Unit, St James Hospital, London UK; GI Surgery Unit, Birmingham General Hospital, UK; Leeds Institute for Minimally Invasive Therapy of Leeds General Infirmary. Prof. Zografos has attended numerous postgraduate courses in UK, Greece, Germany and the USA on the topics of Therapeutic applications of lasers, Head and Neck Surgery, Advanced Trauma Life Support, the Sentinel Node Course, Surgical Oncology, Breast Cancer and Minimal invasive breast biopsy.

He has been awarded a scholarship from the Onassis Foundation for training in breast and endocrine surgery (1988) in the Queen's Medical Centre, Nottingham, UK, and a National Institute of Health Grant for training in Surgical Oncology, Roswell Park Memorial Institute Buffalo, New York, USA (1991). Prof. George Zografos has had the positions of a consultant in General Surgery and a Lecturer in General Surgery at the Medical School of University of Athens (1992), and an Assistant Professor in General Surgery, Medical School, University of Athens (1996).

Apart from being a reviewer in 10 international scientific journals, Prof. George Zografos has 250 papers published in peer-review journals. He has been cited 850 times, and has also held 28 oral and 78 poster presentations at international congresses, together with 190 oral and 194 poster presentations at local Greek conferences. He has participated in 15 clinical trials, and has written 5 chapters in international and 11 chapters in Greek medical books.

Prof. George Zografos has established a European accredited Breast Unit in the 1st Propaedeutic Department of Surgery in Hippocratio General Hospital in Athens, which includes the participation of specialists of all disciplines, covering all aspects of breast cancer. More than 200 newly diagnosed cases of primary breast cancer are coming under its care each year. Junior staff, medical students and visiting doctors are being taught there, regular audit meetings designing and amending protocols are held, and several population breast-screening programmes in various Greek towns have been designed there. Prof. Zografos is the National Representative of Greece in the European Committee for evaluating and funding research protocols, the National Representative of Greece in the New European Surgical Academy (NESA), as well as a member of many committees supporting the Greek Ministry of Health, and a member of the Scientific Committee of many International and Greek Conferences.







**Dr. Yordan Yordanov**

## **Supermicrosurgery for Treatment of Postoperative Lymphedema: What We Know and What We Don't?**

Postoperative lymphedema is the main late side effect of the oncological treatment in cancer survivors. It occurs as a consequence of scarring or injury of otherwise normal lymphatics following ablative surgery and/or radiation exposure and is the most common cause of lymphedema in the developed countries. Although the mainstay of lymphedema treatment is non-surgical, a number of surgical techniques and approaches have been described. However, there is currently no consensus on patient selection, type of procedure, timing of intervention, or postoperative management. During the past ten years supermicrosurgical techniques have been used to connect collecting lymphatics with subdermal veins- so called lymphaticovenous bypass. Three years ago the first supermicrosurgical intervention in Bulgaria was performed.

In the present study a brief review of the main surgical techniques applied for treatment of the postoperative lymphedema was made. A special accent is put on the most contemporary approach-lymphaticovenous bypass. A report on the first cases in Bulgaria of supermicrosurgical lymphaticovenous procedure is made. Beside the treatment protocol, indications and outcomes, a special emphasis is put on the organizational, administrative and institutional pitfalls which the author faced organizing and performing the surgeries.

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Dr. Yordanov is a Board-Certified plastic surgeon and practices at the Uni Hospital- Panagyurishte and in his private practice in Sofia, Bulgaria. Dr. Yordanov performs all types of plastic surgery and specializes in facial and breast aesthetic and reconstructive surgery and microsurgery.

Dr. Yordanov has a PhD degree cum laude in plastic surgery with European Mention by the Complutense University of Madrid, Spain. He is a fellow of the European board of Plastic Reconstructive and Aesthetic Surgery (EBO-PRAS) and a member of the Spanish Society of Plastic Reconstructive and Aesthetic Surgery (SECPRE) and the American Society for Aesthetic Plastic Surgery (ASAPS).

Dr. Yordanov has been trained in Spain, Belgium and USA. He is an author of over 50 scientific articles in national and international renowned journals, two monographs and a co-author in a Plastic Surgery manual book for students in Spanish.

## Dr. Assia Konsoulova



### Issues with anticancer drug availability and access

Cancer incidence is increasing worldwide not only because of aging of the population but as well as the processes of screening, diagnosis and anticancer treatments are continuously evolving. As a chronic condition, frequently with long years of duration, treatment of cancer leads to social and financial burden for the society due to the increased non-medical and health-care necessities of cancer patients and the need of acute and maintenance medicines with adequate and regular supply. Financial issues in oncology are of raising concern because of the significant cost of emerging medicines, frequently unaffordable by National health systems, notably in countries with lower economic development level such as Bulgaria.

Issues with availability and access of anticancer drugs are valid both for expensive and non-expensive drugs and are frequently officially underreported. The disparity in access to anticancer drugs not only amongst countries, but also within Bulgaria is discussed as it may eventually lead to worsening of the patient outcomes.


## Dr. Yavor Drenski



### Personalized Medicine – What is the Situation in Bulgaria?

“The right medicine at the right dose at the right time for the right patient.” The Bulgarian patient is also familiar with this definition of the personalized medicine, and in full compliance with the global trends, the main part of the personalized medicine in Bulgaria is in the field of oncology, oncohematological diseases as well as lung cancer, colorectal cancer, breast cancer, ovarian cancer, malignant skin cancer, etc. Most of the registered target therapies are available for the Bulgarian patient and the treatment (mainly in oncology) is free of charge for the patient, and reimbursed by NHIF. Innovative solutions for the treatment of infectious, cardiological and a number of rare diseases are also present. An integral part of the personalized therapy is to carry out a concomitant diagnostic test that enables a prognosis on the effect of a particular treatment on the patient, and making an informed decision to apply the most effective one, consistent with the patient’s molecular profile and disease. In Bulgaria only some of these mandatory tests are being reimbursed by the NHIF. This type of diagnosis is performed in several specialized laboratories in the country, but there are still no clear





criteria that these structures must meet and centralized quality control of the tests they perform. This is also one of the main problems in the field of personalized medicine in Bulgaria. Another shortcoming is the insufficient awareness and necessity of raising the qualification of the employees in our healthcare system as a whole. A deficiency of specialists in the field of molecular diagnostics (pathology, molecular biology, genetics) is also present.

Another problem is the lack of adequate statistical analyzes for the medical-economic effect of applying the personalized medicine in Bulgaria.

A major participant in the attempt to solve these problems at the national level is the Bulgarian Association for Personalized Medicine (BAPEDED), whose mission is to help to better understand, adopt and implement the concept, services and products of personalized medicine in favor of patients and healthcare system. Our efforts are aimed at raising awareness of all aspects of personalized medicine, finding sustainable solutions and creating a working mechanism for its application, because “Every patient is important!”.

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Dr. Yavor Drenski was the executive director of Tokuda Hospital Sofia from January 2011 until July 2016. He has been a team member of the Japanese hospital since its foundation and he was consecutively the administrative director (2005 - 2009) and the medical director (2010 – 2011) of the hospital.

Dr. Drenski graduated in medicine from Medical University, Sofia, in 1992. He continued his education with a specialization in Obstetrics and Gynaecology. He worked as a physician for eight years, three of which in Libya.

Dr. Drenski graduated from the master's degree programme in Healthcare Management in 2009, he holds a master's degree in Finance from 2003, he has several specializations in the field of hospital management and hospital finances. He specialized in the USA, Switzerland, Hungary, Great Britain, Japan, and other countries.

From 2000 until 2005, Dr. Drenski was an international consultant in healthcare for global companies such as Bearing Point (USA), 3M, Deloitte Touche Tohmatsu, and others.

From 2002 until 2004, he was head of the Hospital Care Department of the National Health Insurance Fund.

During the Founding Assembly of the National Private Hospitals Association, on 16 February 2013, he was elected as a chairman of the organization that unifies the private healthcare institutions in Bulgaria.

In 2015, Dr. Yavor Drenski received the award “Hospital Manager of 2015” during the National Medical Awards. In November 2015, he received the award “Manager of 2015” in the campaign “Junior Medical Specialist”, organized by the Standart newspaper, Darik Radio, and the Ministry of Healthcare in order to actively support the development of young physicians and healthcare professionals.

On 3 October 2016, he was elected as a chairman of the Administrative Board of the Bulgarian Association for Personalized Medicine.

From 01.11.2016 Dr. Yavor Drenski is a consultant at the Hospital “St. Sofia”.



## Dr. Marchela Koleva



Dr. Marchela Koleva graduated from the Medical University in Sofia in 1992. From 1995 till 2012, she has worked and specialized in Internal medicine and in Medical oncology at Queen Joanna University Multiprofile Hospital for Active Treatment in Sofia, Bulgaria. She has also worked in the Department of Medical Oncology at Serdica Hospital in the period June 2012 - April 2013. Dr. Koleva headed the Department of Medical Oncology at Sofia Med Hospital in Sofia 2013-2015. Currently she is the Head of the Department of Medical Oncology at Queen Joanna University Multiprofile Hospital for Active Treatment.

Dr. Marchela Koleva has different specializations in oncology in Austria, Belgium and the UK.

She is a member of a number of European professional organizations (ESMO) as well as of the Bulgarian Medical Society, Bulgarian Oncology Scientific Society, BUON, Young Oncologist Club Bulgaria, Bulgarian Society of Oncology, and the Society of Interventional Oncology. She has specific interests in the medical treatment of solid tumors, having served as an investigator in more than 25 multicenter clinical trials for treatment of solid tumors (as a principal investigator in 10 of them). She has issued 3 monographs and has participated in the preparation of 2 textbooks of medical oncology.

Dr. Koleva has over than 23 publications in the field of oncology and she is a co-author of the Victoria program for rehabilitation of patients with lymphostasis.

Dr. Marchela Koleva speaks three foreign languages - Russian, English, and Spanish.

## Dr. Qaisar Siraj




### **PET/CT in Breast Cancer: Challenges and Unsolved Issues**

Positron Emission Tomography with Computed Tomography (PET/CT) is increasingly becoming a credible method for investigating patients with breast cancers. This hybrid structural-functional imaging technique allows examination of extraaxillary nodes, chest, abdomen, and bone in a single session. Despite its many distinct advantages, the limited spatial resolution of the technique results in a lower sensitivity for the detection of very small tumours and the heterogeneity of metabolic activity in the primary tumours curtail its widespread use currently.

Recent developments in instrumentation and the introduction of new receptor-specific PET radiotracers have considerably improved the diagnostic yield of this combination technique in the primary diagnosis and for staging and follow-up. The higher resolution of the dedicated positron-emission mammography (PEM) systems now allow early detection of very small primary breast tumours even in patients with dense breasts and in younger patients. Though





currently not recommended for the staging of early breast cancer without nodal disease, an initial PET/CT may be useful when there is a high risk of metastases. PET/CT is valuable in staging patients with locally advanced breast cancer, and there is increasing evidence for a substantial yield of PET/CT in stage IIB and IIIA breast cancers. PET/CT may replace conventional imaging methods for staging and is useful for detecting recurrence and for restaging. 18F-sodium fluoride positron emission tomography/CT (NaF-PET/CT) has a very high sensitivity for the detection of breast cancer bone metastases compared with the conventional bone scan and CT screening. 18F-fluoroestradiol PET imaging allows measuring breast cancer estrogen-receptor expression and can predict the tumour response to endocrine therapy.

Molecular and functional imaging in breast cancer is continually evolving and improving and is increasingly providing early information on the underlying biology of individual breast cancers and helps in evaluating potential treatment strategies through the introduction of biomarkers for initial evaluation of treatment effects. Molecular and functional PET/CT imaging of the breast will likely alter clinical practice in breast cancer through early and specific diagnosis, staging and therapy response assessment.

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#### **CURRENT PROFESSIONAL APPOINTMENTS**

- Consultant in Nuclear Medicine & PET-CT: Farwania Hospital Kuwait & Molecular Imaging Centre Kuwait
- Examiner Asian Board of Nuclear Medicine: Asian School of Nuclear Medicine
- Editor-in-Chief/Founding Editor: Pakistan Journal of Nuclear Medicine
- Associate Editor: Asia Oceanic Journal of Nuclear Medicine & Biology

#### **MEDICAL EDUCATION**

Ph.D in Nuclear Medicine, 1993

Royal Free Hospital School of Medicine, University of London

M.Sc in Nuclear Medicine, 1984

Royal Free Hospital School of Medicine, University of London

Grading in Nuclear Medicine 1982, AFM College, Rawalpindi

Bachelor of Medicine & Surgery, M.B;B.S, 1977, Dow Medical College, Karachi University

#### **AWARDS & HONOURS**

- Prize for Scientific Posters, Gulf Nuclear Medicine Conference 2013
- Chairman's Award for Excellence, Portsmouth Hospitals NHS Trust, 2005
- Clinical Excellence Award (Level 4), Portsmouth Hospitals NHS Trust 2005
- Clinical Excellence Award (Level 3), Portsmouth Hospitals NHS Trust 2003
- Distinguished Alumnus, Dow Medical University, Karachi, 2004
- Best Poster Award, British Nuclear Medicine Society, 2001
- Distinction Award, Best publication, Society of Nuclear Medicine, 1997
- Distinction Award for Ph.D thesis, University of London, 1993.
- Travelling Fellowship, British Nuclear Medicine Society, 1991


#### **PROFESSIONAL EXPERIENCE (Past 10 Years)**

Consultant in Nuclear Medicine & PET-CT, Farwaniya Hospital, 2011- present

Hon. Consultant in Nuclear Medicine & PET-CT, University College Hospital,

Consultant in Nuclear Medicine, King Fahad Specialist Hospital, Dammam, 2009-2010





Consultant & Lead Clinician in Nuclear Medicine, Portsmouth Hospitals, UK, 1999-2009  
Locum Consultant in Nuclear Medicine, St. Peter's Hospital Chertsey, UK, 1999  
Locum Consultant in Nuclear Medicine, Great Ormond Street Hospital, UK, 1998-1999  
Locum Consultant in Nuclear Medicine, Addenbrooke's Hospital, Cambridge, 1998-1999  
Locum Consultant in Nuclear Medicine, Charing Cross Hospital, London, 1997-1998  
Senior Research Associate, UMDS (Guy's & St. Thomas's Hospitals), London, 1997-1998  
Visiting Consultant, St. Bartholomew's Hospital, London, 1996-1997  
Consultant in Nuclear Medicine, Nuclear Medical Centre, AFIP, Rawalpindi, 1995-1996  
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Consultant in Nuclear Medicine (NHS sessions 2), Royal London Hospital, 1993-1994  
Consultant in Nuclear Medicine (NHS sessions 4), St. Bartholomew's Hospital, London, 1993-1994  
Dr. Qaisar H. Siraj has more than 74 scientific publications – editorials, book chapters and articles in journals like Lancet, Journal of Nuclear Medicine, European Journal of Nuclear Medicine Technology, Journal of Rheumatology, Journal of Pakistan Medical Association, etc.

## Dr. David Pinto

### Sentinel Lymph node biopsy in Breast Cancer – Challenges and Controversies

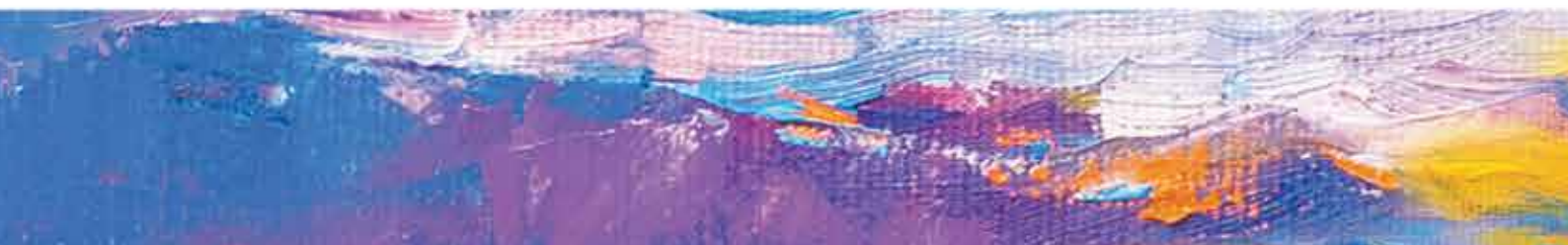
Axillary lymph node status is one of the most important prognostic factors in patients with primary breast cancer and provides critical information for treatment guidance. Axillary management for early-stage breast cancer patients continues to evolve, with the goal of optimal oncologic safety coupled with nominal surgical morbidity.

Strong evidence supports the use of sentinel lymph node biopsy (SLNB) in the clinical negative axilla, with less morbidity and the same oncological value when compared with axillary lymph node dissection (ALND).

Although SLNB indication is very well established in node-negative early breast cancer patients, the increasing use of neoadjuvant therapy with very good response rates in some biological subtypes of disease, the amazing development of radiotherapy techniques, together with several powerful clinical trials that support alternative protocols for axillary management, this arouse the challenge to explore more indications for this technique.

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Dr. David Alexandre Gomes Pinto is an oncoplastic breast surgeon nuclear currently working in the breast unit of Champalimaud Cancer Center. He was born 1980 in Lisbon, Portugal and graduated the Medical School - Faculdade de Ciências Médicas, Universidade Nova de Lisboa in 2004. He got his General Surgery Qualification (Portuguese Medical Association) in 2012 and is Breast surgeon certified (UEMS) since 2015.







**Dr. Valkan Ivanov**

## **Screen detected breast cancer – Micro tumors with macro approach! Are we acting or we are hiding?**

Breast Screening Programmes in the advanced EU countries and UK have proven the benefits of early stage breast cancer diagnosis and treatment. That fact inevitably leads to better prognosis and increased survival rate. The screening in Bulgaria is a myth and we should aim to make it active, governmental engagement. Most of the screen detected or the interval tumours are impalpable and difficult to operate with a good cosmetic and secure oncological outcome. The UK guidelines suggest, that a complete oncological diagnosis of all the invasive tumours also includes Sentinel Lymph Node Biopsy. That fact leads to a mirror surgical demand – the need of localised wide local excisions and a precise radiology department with a qualified breast radiologists and also trained oncoplastic surgeons. That technique reduces the number of operations, relates to a secure oncologically adequate approach and excellent cosmetic outcome. The wire guided wide local excision combined with or without SLNB and provided by using oncoplastic techniques is the solution of the problem that we aim to achieve.

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Dr. Valkan Ivanov is a Bulgarian specialist in the field of general surgery and oncoplastic breast surgery, currently working as a General and Breast Oncoplastic Consultant at Acibadem City Clinic, Varna, Bulgaria.

Dr. Ivanov was born in 1977. He graduated the Medical University in Varna as a medical doctor and then got his specialty in General surgery in the same university in 2011. He holds a GMC License Number and is registered in the Swedish Medical Council – Medicine and General Surgery.

Dr. Valkan Ivanov has a rich carrier both in the pharmaceutical industry having worked for GSK, Novo Nordisk and Novartis, and as a general surgery and breast surgery consultant in a number of hospitals in Wales and England in the period 2012-2017. In Bulgaria, he has also had experience working in the Naval Hospital (2004-2020) and Euro Hospital (2010-2012) in Varna, as well as for Varna branch of Acibadem City Clinic (since October 2017).

Dr. Ivanov has had teaching responsibilities at Bristol University in 2014 and as an Assistant at the General and Mini-invasive Surgery Clinics between 2005 and 2010. He has also done 3 presentations at the 17th World Congress of the International Association of Surgeons and Gastroenterologists and Oncologists – Bucharest, Romania, and also co-chaired a scientific session at that event in 2007. He has been a co-author of 6 scientific publications as well.

Dr. Valkan Stoyanov Ivanov speaks 2 foreign languages – English, and Russian.

## Dr. Veneta Stoykova



### Management of Pregnant Patients with Breast Cancer: Gynecology Aspects

Increasing trend for women to delay childbearing lately leads to higher rate of pregnancy complications. It is also related to bigger number of neoplastic diseases diagnosed during pregnancy. Breast cancer is the most common malignancy diagnosed during pregnancy. It affects every 1 in 3000 pregnancies and this number is growing lately. Though possibly harmful to the fetusmaternal treatment is essential due to the serious prognosis of the disease. We will discuss the contemporary trends in treatment of breast cancer during pregnancy and the changes of pregnancy follow up and management of these patients. What, when and why or why not are the most important questions we have to answer. The aim of the interdisciplinary approach is to deliver a healthy term baby together with the best possible treatment for the particular patient.

Dr. Veneta Stoykova is a gynecologist who works in SBALAG Maichin Dom in Sofia, Bulgaria and is also a university lecturer in the same hospital.

Dr. Stoykova graduated the Medical University in Sofia in 2002 and specialized in Obstetrics and Gynecology in the period 2003-2008. She got her specialty in August 2008 and later on acquired a Doctor's degree in Obstetrics and Gynecology in February 2012. In 2015, Dr. Stoykova graduated the Medical University in Sofia with a second specialty - Health Management and Public Healthcare.

Dr. Veneta Stoykova started her career as a doctor in the emergency department of Sofia region. Later on, she moved to MBAL Vita, where she worked for 2 years from 2004 to 2006. She has also had a 7-year experience working as a doctor in St. Dimitar Medical Centre (2008-2015). Dr. Stoykova is a member of Bulgarian Medical Association, Bulgarian Scientific Society of Obstetrics and Gynecology, ISUOG, etc. She has more than 13 specializations and training courses in different clinics in Portugal, Greece, the Netherlands, UK, Italy, Serbia, and Bulgaria.

Dr. Veneta Radostinova Stoykova speaks Russian and English as foreign languages.

## Dr. Assia Konsoulova



### Breast Cancer during pregnancy

Breast cancer occurring during pregnancy is a condition that affects not only the patient but the unborn baby as well. Termination of the pregnancy remains a worrisome clinical practice despite the fact that it does not improve the clinical outcomes of the women and should thus be avoided if possible. The recommendations for diagnosis, staging and further



treatment are summarized and the specific considerations due to the pregnancy are presented. The patient management consists of regular obstetrical assessment, aiming to avoid preterm/iatrogenic delivery until sufficient fetal maturation without compromise in the cancer treatment. Toxicities of the diagnostic management (Rx, contrast substances, etc.) as well as treatment toxicity and complications (hematologic toxicity, infections, potential teratogenicity, etc.) are also avoidable. Natural delivery as in healthy women is recommended avoiding the period of the chemotherapy toxicity nadir. Treatment options as (neo)adjuvant chemotherapy (anthracyclines and taxanes) with some restrictions and limitations (e.g. trastuzumab, tamoxifen, etc.) are also discussed.



**Dr. Rossitza Krasteva**

## **Male Breast Cancer**

Male breast cancer (MBC) is a rare disease compared with female breast cancer and our current understanding regarding breast carcinogenesis in men has been largely extrapolated from the female counterpart.

The causes, optimal treatments, and medical/psychosocial sequelae of breast cancer in men are poorly understood. A systematic literature search by using PubMed (<http://www.ncbi.nlm.nih.gov/pubmed/>), was carried out to provide a synopsis of the current research in the field of MBC genetics, epigenetics and ethics.

As in women, three classes of breast cancer genetic susceptibility (high, moderate, and low penetrance) are recognized in men. However, genes involved and their impact do not exactly overlap in female and male breast cancer. Epigenetic alterations are currently scarcely investigated in MBC, however, the different methylation and miRNA expression profiles identified to date in female and male BCs suggest a potential role for epigenetic alterations as diagnostic biomarkers. Overall, much still needs to be learned about MBC and, because of its rarity, the main effort is to develop large consortia for moving forward in understanding MBC and improving patient management on a perspective of gender medicine.

Further research is needed to address gaps in knowledge pertaining to care of male breast cancer patients and survivors.

## Dr. Flora Zagouri



### Management of Triple Negative Breast Cancer


Triple negative breast cancer accounts for 15-20% of all cases of invasive breast cancer and is defined by the absence of estrogen receptors, progesterone receptors and human epidermal growth factor 2 (HER2/neu) overexpression or/and amplification. TNBC presents an aggressive disease that is characterized by younger age and advanced stage at diagnosis, high rates of distal visceral metastasis, increased mortality after first recurrence and poor outcome. Furthermore, triple negative breast cancer consists of tumors with increased sensitivity in chemotherapy, even if most patients will relapse in the first three years from diagnosis. Chemotherapy constitutes the only standard of treatment in TNBC and is based mostly in anthracycline and taxane agents. However, patients experience several serious adverse events and become soon resistance in chemotherapy. Thus, the design of new targeted therapies is imposed for improved the outcome of this malignancy, although this is difficult due to the high molecular heterogeneity of the disease. Olaparib, a PARP inhibitor, is the first approved target therapy in triple negative breast cancer in the setting of BRCA mutated subtype. Met inhibitors and immunotherapy agents especially anti-PD-1/PDL-1 checkpoints inhibitors are in advanced stage of clinical trials showing encouraged result in triple negative breast cancer management and overall survival. Finally, a new field in TNBC targeted therapy is the use of AR (androgen receptors) inhibitors (enzalutamide and abiraterone) in a subtype of TNBC that presents a positive expression of androgen receptors.

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She obtained her medical degree from the National and Kapodistrian University of Athens in 2003, completed a residency in medical oncology at the Alexandra Hospital and a fellowship in oncology at the University of Vienna, Austria (AKH Hospital – Comprehensive Cancer Center). Dr Zagouri is a member of numerous scientific societies and has authored more than 200 publications in peer-reviewed journals, as well as numerous abstracts and several textbook chapters primarily focusing on breast cancer. She has more than 2000 citations. She is a journal reviewer for several journals and evaluator of research proposals submitted to European Research Council. Dr Zagouri is an Associate editor in several journals. She has participated in more than 20 clinical trials either as Sub-investigator or as Principal investigator mainly focused on breast cancer.





## Boehringer Ingelheim Symposium: The Modern Approach to the Diagnosis and Treatment of NSCLC

Activating mutations in the epidermal growth factor receptor (EGFR) are known to be a driver of non-small cell lung carcinoma (NSCLC), and tyrosine kinase inhibitors (TKIs) that target these mutations are currently standard of care for first-line therapy in patients with EGFR mutation positive (EGFRM+) NSCLC. However, many patients with EGFRM+ disease eventually develop acquired resistance to these therapies, which most commonly occurs via T790M mutation. The clinical development of 3rd generation TKIs provides additional treatment options for these patients and can extend the chemotherapy-free interval. For clinicians seeking to further improve patient outcomes, this progress in clinical development raises questions about the optimal sequence of EGFR TKI therapies.

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Dr. Maya Gottfried, serves as Head of the Lung Oncology Unit at the Meir Medical Center in Kfar-Saba, Israel. She is also associate professor of the medical Faculty of Medicine at Tel Aviv University since 1994. Dr. Gottfried serves as Member of Medical Advisory Board at Rosetta Genomics, Ltd. Dr. Gottfried has earned distinction for her extensive clinical and academic experience. She is a specialist in medical oncology and radiotherapy and she serves as member of the Israel Society of Clinical Oncology & Radiotherapy, the European Association for Cancer Research, the European Society of Medical Oncology and the International Association for the Study of Lung Cancer. She has been a valued participant in many clinical trials, several as principal investigator, and has made presentations in major scientific meetings, including the 21st ESMO Congress in Vienna, the ASCO meeting in New Orleans, the 11th World Conference on Lung Cancer in Barcelona, the 1st Congress of Lung Cancer Experts in Hamburg and the Global Cancer Group in Lisbon. Dr. Maya Gottfried is the author more than thirty scientific papers and publications, including the section in the textbook of oncology. Research interests of Dr. Maya Gottfried are the research of non-small cell lung cancer, clinical cancer research at second and third stages.





**Dr. Assia Konsoulova**



## **Changing the treatment paradigm in HR+/HER2- mBC: The impact of Ibrance (Palbociclib) and the new CDK 4/6 generation**

Advanced/metastatic breast cancer (ABC / MBC) is characterized by high mortality rates that have remained relatively stable for the last years - an analysis of SEER database for 1975-2014 reported an overall 5-year relative survival rate of 27% for stage IV BC overall. There have been numerous achievements in the treatment of advanced disease in the last decade with incremental benefits in some BC subsets such as the HER2 positive BC. In luminal subtypes, several endocrine therapy (ET) options have proven to be effective in the advanced setting: they include the selective estrogen receptor modulators Tamoxifen, aromatase inhibitors (anastrozole, letrozole, exemestane) with or without ovarian ablation according to the menopausal status and the selective estrogen receptor downregulator Fulvestrant. Current guidelines are generally based on studies in postmenopausal women, although in recent years more and more trials start to include premenopausal patients. As stated by the international ABC/MBC guidelines (ASCO and ESO-ESMO), in the absence of visceral crisis and/or life-threatening symptoms or need for rapid symptom control, ET is given preference as a treatment modality. For postmenopausal women, AIs are the preferred first-line endocrine therapy, with or without the cyclin-dependent kinase inhibitor. As second-line therapy, fulvestrant may also be considered with the addition of palbociclib. Premenopausal patients should be treated with the same treatment options as postmenopausal women as long as they are rendered post-menopausal by additional ovarian ablation. The addition of a CDK4/6 inhibitor to an aromatase inhibitor, in patients naïve or pre-exposed to ET, provided a significant improvement in median PFS (~10 months), with an acceptable toxicity profile, and is therefore one of the preferred treatment options. OS results are still awaited and the QoL is comparable to that with ET alone.



The image shows a notebook cover. The top and bottom edges feature a textured, abstract pattern in shades of blue, purple, and yellow. The central portion of the cover is white and contains horizontal ruling lines, typical of a notebook. The word "Notes" is printed in a bold, black, serif font on the left side of the white area.

The image shows a notebook page with a decorative border at the top and bottom. The top border is a dark blue and red abstract pattern. The bottom border is a similar abstract pattern in shades of blue, purple, and yellow. The central area of the page is white and contains horizontal ruling lines. The word "Notes" is written in white, serif font on the top blue background.



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