VI INTERNATIONAL MEETING OF
YOUNG ONCOLOGIST CLUB BULGARIA

МладОнколог

NEW ASPECTS IN THE TREATMENT OF COLORECTAL CANCER AND IMMUNOTHERAPY OF SOLID TUMORS.

PLOVDIV, MAY 13-15, 2016

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PROGRAMME

13 May

13.00 – 19.00	Registration
14.45 – 15.00	Opening, R. Krasteva

FIRST SESSION (INDUSTRY SYMPOSIA)
Moderators: H. Spasov, P. Balikova

15.00 – 15.45	Amgen Symposium
15.45 – 16.05	Astellas Lecture
16.05 – 16.35	Poster Session
16.35 – 17.00	Coffee Break
17.00 – 18.00	Sanofi-Aventis Symposium
18.00 – 18.20	Boehringer Ingelheim Lecture
18.20 – 18.50	Roche Lecture
18.50 – 20.00	Free time
20.00 – 22.00	Dinner

14 May

SECOND SESSION: IMMUNOTHERAPY OF SOLID TUMORS
Moderators: A. Konsulova, Al. Gerassimov

09.00 – 09.30	Introduction to Cancer Immunotherapy. Sarcoma Immunotherapy: Past Approaches and Future Directions, T. Brodowicz
09.30 – 09.50	Radiolabeled Monoclonal Antibodies in the Treatment of Solid Tumours, Q. Siraj
09.50 – 10.10	Role of Immunotherapy in Breast Cancer, A. Konsulova
10.10 – 10.30	The Immuno-Oncology Revolution: Immune Checkpoint Inhibitors in the Treatment of Lung Cancer, S. Rothschild
10.30 – 10.50	The Evolving Role of Immunotherapy in the Treatment of Malignant Melanoma, N. Chilingirova
10.50 – 11.10	Coffee Break
11.10 – 11.40	Non-specific Cancer Immunotherapy, Z. Krastev
11.40 – 12.00	New Diagnostic Paradigm in the Current and the Future Personalized Cancer Treatment – a Touch of Overcoming the Resistance to Treatment - Case Reports, B. Petrov
12.00 – 13.00	Case Studies & Discussion (cases to be presented by young oncologists)
13.00 – 14.00	Lunch

THIRD SESSION: COLORECTAL CANCER
Moderators: M. Petrova, N. Chilingirova

14.00 – 14.20	Targeted Therapies in Colorectal Cancer According to the Molecular Profile of the Tumors, G. Samelis
14.20 – 14.40	^{18}F-FDG PET/CT in Staging and Follow–up of a Patient with Colorectal Cancer, J. Mihailovic
14.40 – 15.10	Surgery for Colorectal Cancer - New Methods Compared with the Old Classic Operations, G. Zografos
15.10 – 15.30	Adjuvant Chemotherapy for Colorectal Cancer - New Aspects, F. Zagouri
15.30 – 15.50	Clinical Challenges in Metastatic Colorectal Cancer: Optimizing Treatment, G. Kurteva
15.50 – 16.10	Coffee Break
16.10 – 16.30	Stereotactic Ablative Radiotherapy (SABR) in Oligometastatic Disease from CRC, U. Ricardi
16.30 – 16.50	Radionuclide Therapy for Liver Metastases from Colorectal Cancer, P. Castellucci
16.50 – 17.10	SPECT-CT Somatostatin-Receptor Scintigraphy in Colorectal NETs, S.Sergieva
17.10 – 17.30	Microbiota, Inflammation and Gastrointestinal Tumors, A. Decheva
17.30 – 18.30	Case Studies & Discussion (cases to be presented by young oncologists)
18.30 – 20.00	Free time
20.00 – 23.00	Dinner

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DR. ROSSITZA KRASTEVA

WELCOME TO THE VI INTERNATIONAL MEETING OF YOUNG ONCOLOGIST CLUB BULGARIA 2016

DEAR COLLEAGUES AND FRIENDS,

On behalf of the Board of Young Oncologist Club Bulgaria, I would like to welcome you to our International Meeting, which we are organizing for a sixth consecutive year. The topics in focus are the new aspects in the treatment of the colorectal cancer and the immunotherapy of the solid tumors.

The colorectal cancer is one of the most common types of cancers. Great progress has been reported in the recent years both in the field of understanding the biology, and in the treatment of this disease. During our meeting, we will present the multi-disciplinary interactions between the various specialties involved in the treatment of this disease. Those include genetics, biology, anatomy, prognostic markers, surgery, medical treatment, radiotherapy, nuclear and imaging diagnostics.

Immunotherapy has revolutionized the treatment of almost every type of cancer. It represents an entirely new class of cancer treatment with unique features, which distinguish it from all other types of cancer therapies. Due to its extraordinary power, memory capacity, and exquisite specificity, the immune system has a central and a universal role in human biology. This type of treatment has the potential to lead to a full and long-time remission in each cancer patient, with minimum side effects.

Our meeting aims at continuing the tradition of excellence and stimulating the interest of the participants towards innovative practices and treatments. I hope that you will find this scientific event both challenging and useful, and you will actively contribute to its success.

DR. ROSSITZA KRASTEVA

AFLIBERCEPT / FOLFIRI IN THE TREATMENT OF METASTATIC COLORECTAL CANCER

The proven clinical benefit from the addition of target therapy with biological agents (anti-EGFR and anti-VEGFR) to the standard chemotherapy regimens for the treatment of patients with metastatic colorectal cancer (mCRC) and the different clinical efficacy, depending on the tumour-specific genome (RAS status), has changed the standards for the treatment of mCRC and today we talk about a patient-individualized therapy in the era of biological agents. Despite the proven benefit to the overall survival and the disease-free survival after the incorporation of anti-EGFR and anti-VEGFR, colorectal cancer remains one of the leading causes of mortality from solid tumours.

The aim of the presentation is to present Aflibercept, a medicinal product of the anti-VEGFR agents, the scientific evidence for its expanded ligand specificity compared to existing agents in the same group, and its positioning in the treatment of patients with mCRC, as well as the available literature data on cross-resistance between the target medicinal agents, which in turn is the basis for selection of a therapeutic sequence in the development of patient-individual therapeutic strategy.

Dr. Rossitza Krasteva Ruseva, 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 has also won a number of fellowships for further training in Bulgaria and abroad, as well as has 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 Yoanna – 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-researcher 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. 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.

PROF. JANET GRUDEVA-POPOVA, MD, PHD

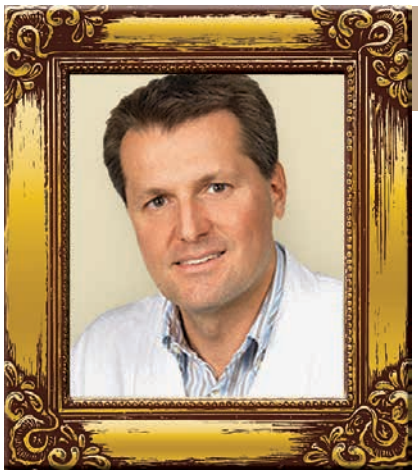
SANOFI-GENZYME IN THE TREATMENT OF PATIENTS WITH SOLID TUMORS

The incidence of oncology diseases in Bulgaria and worldwide is growing every year. Regardless of the significant therapeutic advances, solid tumors remain one of the leading causes of mortality. The Sanofi-Genzyme portfolio includes medicinal products for the treatment of various solid tumours – the prostate carcinoma (Cabazitaxel), the colorectal cancer (Aflibercept), and the thyroid carcinoma (Caprelsa and Thyrogen).

Various advanced treatment options in one line of treatment, for a particular location, and based on an individual patient profile are aimed at maximizing disease-free survival together with an acceptable quality of life. Given the diverse range of medications with different mechanisms of action the treating physician should be able to make the right therapeutic decision, based on evidence-based medicine.

The focus of this symposium is the approach for a most effective sequence of second-line therapy in patients with metastatic colorectal cancer as well as in patients with metastatic castration-resistant prostate cancer.

Professor Janet Grudeva-Popova, MD, PhD, is a deputy director DTD - Base 1, University Hospital "St George", Head of the Department of Medical Oncology at the University Hospital St. George and Vice Dean on Research in the MF of PMU. She graduated medicine in 1981 at the Medical University - Plovdiv, Bulgaria as country best graduate with honours and received the national prize "Golden Hippocrates." She got a specialty in Internal Medicine in 1988, one in clinical haematology in 1991, one in medical oncology in 2010 as well as a Master's degree in Economics and Health Management at the University of Plovdiv in 2002. She had her PhD degree in medicine in 1997 and her professorship in the MU of Plovdiv in 2013. Prof. Grudeva has over 110 publications in Bulgarian and international journals, together with extensive experience in teaching and research, as well as in international clinical trials.



PROF. THOMAS BRODOWICZ

Thomas Brodowicz is an Associate Professor of Hematology and Oncology, Senior Consultant and Program Director of Bone- and Soft Tissue Sarcomas at the Clinical Division of Oncology, Department of Medicine 1, Medical University Vienna, Austria. In addition he serves as Director of the Central European Cooperative Oncology Group (CECOG, www.cecog.org).

Thomas Brodowicz completed his medical training at the University Hospital Vienna. His recent clinical research activities cover a wide range of cancer therapies, with particular focus on management of clinical trials in breast cancer, colorectal cancer, NSCLC, GIST, soft tissue sarcoma, prostate cancer and gastric cancer. Thomas Brodowicz is a member of the American Society of Clinical Oncology (ASCO). He has published 73 scientific papers and 138 abstracts.

DR. RADOSLAV MANGALDZHIEV

THE PLACE OF SYSTEMIC CHEMOTHERAPY IN THE TREATMENT OF METASTATIC PROSTATE CANCER

Radoslav Mangaldzhiev[1]; Varbanova V[2], PhD
The Place of Systemic Chemotherapy in the Treatment of Metastatic Prostate Cancer
1 Specialized Hospital for Active Treatment of Oncology EOOD, Sofia
2 Sanofi-Aventis, Bulgaria EOOD

Prostate cancer (PC) is second in morbidity and mortality from neoplasms among men, which defines the great social and medical interest in the treatment of these patients. Although hormone therapy is the standard of treatment in the initial therapy of the metastatic PC, the natural evolution of the disease to castration resistance is inevitable. The latter determines the attempts of various research teams for the incorporation of new therapeutic strategies to slow progression, improve quality of life and / or reduce the complications, associated with the metastatic PC.

The positive results of two large randomized trials, phase III (STAMPEDE and CHAARTED) altered the therapeutic approach with early involvement of systemic chemotherapy in patients with metastatic hormone-sensitive prostate cancer. By registering second generation taxanes (Cabazitaxel), AR-target agents, immuno- and radio-therapy, the therapeutic options for patients with castration-refractory PC (mKRPK) were significantly enriched. Literary data from retrospective analyses examining the efficacy of sequential administration of three available therapeutic options after Docetaxel (Cabazitaxel, Abirateroneacetate and Enzalutamide), prove the importance of the correct sequence of therapy in terms of overall survival and progression-free survival. However, there is still no common standard for the optimal treatment sequence in mKRPK and it is determined by the treating physician depending on the individual clinical judgment, based on the specific patient and disease characteristics.

The purpose of the presentation is to present the literature data for the place of systemic chemotherapy in the treatment of patients with metastatic prostate cancer and the current data for the therapeutic effectiveness of the various sequences of therapy after treatment with Docetaxel.

Dr. Radoslav Mangaldzhiev graduated medicine in the Medical Academy in Sofia in 1996. His whole career is in the field of the treatment of patients with malignant diseases, working subsequently in the Regional Cancer Dispensary Sofia City (1996-2011), and in the Clinic of medical oncology at University Hospital Queen Joanna-ISUL, Sofia (2011-2014 AD). Since 2014, he serves as the Head of medical oncology department at SBALOZ Sofia city EOOD. Dr. Mangaldzhiev is a member of Bulgarian Dermatological Society, Bulgarian Cancer Society, BUON and ESMO. His postgraduate training included the acquisition of two medical specialties - Dermatology (2003) and Medical oncology (2008). He has over 13 years of experience in clinical trials including more than 15 clinical trials in breast tumours, colorectal tumours, lungs and prostate.

DR. VICTORIA VARBANOVA

Dr. Victoria Varbanova graduated medicine in 2006 at the Medical University of Sofia. She got a scientific degree "Doctor of Medicine" in 2010, and since 2015 holds the position of a head assistant professor at the National Hospital for Active Treatment of Hematologic Diseases Sofia. She has over 50 presentations at national and international events, as well as 9 publications in Bulgarian and international journals. Dr. Varbanova got a specialty in clinical haematology in 2014. Currently, Dr. Varbanova works as head assistant professor at NSBALHZ and as a medical advisor in the oncology department of Sanofi-Aventis.

DR. BOZHIL ROBEV

DURATION OF CHEMOTHERAPY IN THE TREATMENT OF METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MKRPK). CASE REPORT AND LITERATURE REVIEW

Bozhil Robev[1];, Varbanova V[2] PhD.
1 Department of Medical Oncology, University Hospital St. Ivan Rilsky, Sofia
2 Sanofi-Aventis, Bulgaria EOOD

Cabazitaxel in combination with prednisone or prednisolone prolongs the overall survival, the disease-free survival and the percentage of patients with a reduction in PSA ≥50% compared to mitoxantron therapy in patients with metastatic hormone-refractory prostate cancer (mKRPK) previously treated with a regimen containing Docetaxel (TROPIC study). Literature data on safety and efficacy of Cabazitaxel after 10 cycles of therapy demonstrated an improvement in the clinical efficacy with the increase in the number of treatment cycles, together with an absence of any effect of the cumulative dose of cabazitaxel on the frequency of adverse events.

CLINICAL CASE: A retrospective analysis of a patient with an mKRPK treated with 16 cycles of Cabazitaxel x 25 mg / m2 q3w + Prednisone after progression upon first-line therapy with Docetaxel.

RESULTS: The follow-up of the patient every four months with testing the PSA and every 6 months of a whole-body scintigraphy of the bones showed SD on bone metastases without grade ≥3 ADRs. A progression of the disease was registered after 16 cycles of therapy Cabazitaxel.

CONCLUSION: The treatment with cabazitaxel in combination with prednisone or prednisolone until PC progression or until an unacceptable drug toxicity is an effective therapeutic approach for the treatment of patients with mKRPK previously treated with a regimen containing docetaxel.

Dr. Bozhil St. Robev graduated medicine in 1993 at the Medical University St. Zagora, after which he worked at the ER in the town of Sliven until 1997. From 1997 till 1999, he specialized in paediatrics at the Medical University of Sofia, then working as a paediatrician in the third workers hospital in Sofia. From February 2005 till December 2014 he worked as an intern in the Sofia City Oncology Dispensary, and from January 2015 till February 2016 as the Head of the department of medical oncology at the University Hospital St. Ivan Rilsky. His research interests are in the field of the neuroendocrine tumours and the tumours of the uro-genital system, in line of which, he has participated in international congresses and has had publications in Bulgarian and foreign journals.

VIOLINA TASKOVA, MD

RANDOMIZED, OPEN LABEL STUDY TO ASSESS THE EFFICACY AND SAFETY OF THE INTRAVENOUS AND ORAL IBANDRONIC ACID FOR IMPROVING THE PERFORMANCE STATUS OF PATIENTS WITH MALIGNANT BONE DISEASE SECONDARY TO SOLID TUMORS AND HEMATOLOGICAL MALIGNANCIES

BACKGROUND AND RATIONALE: The metastatic bone disease, characterized by osteolytic bone destruction is the most common manifestation of recurrent metastatic carcinoma. Up to 30% of women with metastatic breast cancer develop the first metastases in the bones, and skeletal diseases are also quite common in patients with prostate cancer, colorectal carcinoma and multiple myeloma at death. Skeletal metastases contribute to increased pain, pathological fractures, hypercalcaemia and marrow infiltration, and they are also an important presage of patients' morbidity, significantly reducing their quality of life. Ibandronate is a highly potent, single-nitrogen bisphosphonate that is available in i.v. and oral formulations. In phase III trials in breast cancer patients, both formulations reduced the incidence of skeletal complications. The question is whether the oral formulation has the same efficacy as the intravenous one for reduction of bone pain and improvement of functional ability in patients with malignant bone disease due to solid tumors and hematological malignancies.

OBJECTIVES: The primary objective of this study is the evaluation of efficacy of intravenous and oral ibandronate formulations for the improvement of the overall performance status of patients with bone disease secondary to various malignant diseases. Secondary endpoints are onset of the reduction of the sum of the points of the most acute pain, according to BPI during the treatment and safety of ibandronate in other malignant diseases, different from breast cancer.

METHOD: Randomized, open, multicentered, two-arm trial of Ibandronic acid in patients with malignant bone disease caused by solid tumors and hematological malignancies. The patients were randomized into A or B therapeutic arms. The A-arm patients received Ibandronic acid amp. 6 mg every 3 to 4 weeks, administered for over 15-minutes infusion. The B-arm patients received Ibandronic acid tabl. 50 mg administered orally by 1 tablet daily. Treatment in both arms has continued 4 months, until occurrence of unacceptable toxicity or withdrawal from the study with 1 month of follow up. The efficacy was determined as pain response (>25% reduction of the points of the most acute pain according to BPI - Brief Pain Inventory) and change in Karnofsky Performance Index (KPI) during the 4-month of treatment. Safety was evaluated through routine adverse event reporting.

RESULTS: From all 97 patients, included in the study, 90 are suitable for subsequent efficacy analysis. From patients successfully ended the treatment 94, 2% have reached pain response (97,85 for arm A and 92,5% for arm B). The difference between both arms is not statistically significant. Mean intensity of pain, decreased continuously over time. A statistically significant reduction in mean pain is registered when comparing the mean intensity of pain at the beginning of treatment and at the end of follow up ($p < 0,001$). At the beginning of treatment average KPI was 74,38 and at the end of follow up was 82, 29. The same trend of gradual increase in the average ratings was observed in both groups. Comparing the average KPI values of the two groups at different points of time showed no statistically significant differences between two arms. That means that patients from both arms have similar change in KPI during the 4-month of treatment. Most early response was monitored at 25th day, and at the latest - on 70th day. The median is 54, i.e. half responded to 54th day and the other half - thereafter. The total number of all observed AEs was 29. Most common of them are hypocalcemia – approximately 20,7% of all AEs, iron deficiency anemia and pulmonary insufficiency - 13,8%. Pain is observed in 3 cases (10,3%). Rest of the AEs were observed only once per AE (3,4%). SAEs - were observed for 5 patients - all of them were not associated with study drug.

CONCLUSIONS: In this study, treatment with intravenous and oral ibandronic acid of patients with malignant bone disease secondary to solid tumors and hematological malignancies resulted in statistically significant reduction of pain and in statistically significant increase in the assessment of Karnofsky Performance Index. There are no statistically significant differences between the two groups in term of pain response and KPI values. Overall the treatment was well tolerated. (ML20713, NCT02561039).

Dr. Violina Taskova is a respected specialist in medical oncology. Her specialties are Oncology and Internal Medicine, and she also has Master's degree in Healthcare Management.

Dr. Taskova carries out oncology consultations and counselling in medical oncology at City Clinic Hospital in Varna. Having experience in treating all types of cancer, she has participated in numerous international clinical projects which offered adequate modern medical treatment to patients.

DR. ANTOANETA TOMOVA

AN OPEN-LABEL, PHASE IV STUDY OF THE EFFICACY, SAFETY AND PHARMACOECONOMICS OF ORAL IBANDRONATE (BONDRONAT) 50 MG IN TREATMENT OF METASTATIC BONE DISEASE

BACKGROUND AND RATIONALE: MBD (Metastatic bone disease, also known as tumour osteolysis or bone metastases) is a common complication of the advanced carcinoma. An average of 70% of the patients with breast cancer develops bone metastases. Approximately 30-40% of the primary metastases are in the bones, and 90% of the patients with this type of cancer have MBD at the time of death. One of the main reasons for this high rate of bone involvement is the affinity of the breast cancer cells to the bones. MBD causes a number of serious clinical complications, including: vertebral and non-vertebral fractures, bone marrow and nerve root compression, hypercalcemia (which may be life-threatening if not treated quickly). Fractures are particularly common, affecting 45-75% of the patients with MBD. Approximately 2/3 of the patients with MBD have bone pain, which is an indication of bisphosphonate therapy. Severe bone pain can reduce mobility and functional abilities of the patient and significantly worsen the quality of life.

Antiresorptive agents such as bisphosphonates are the only known treatment that affects the causes of MBD and its complications.Bisphosphonates affect the pathophysiological mechanisms of MBD development. Bisphosphonates act by selectively inhibiting the osteoclast activity, thus reducing bone resorption. Bisphosphonate therapy affects the bone pain and prevents MBD complications. Clinical studies phase III shown comparable clinical benefit of intravenous and oral Ibandronate in patients with MBD.

OBJECTIVES: The primary objectives of this study are to evaluate safety, tolerability and therapeutic response to oral

ibandronate (Bondronat 50 mg) administered once daily in patients with metastatic bone disease and breast cancer. The secondary objectives of this study are to evaluate improvement of QoL (Quality of Life) and cost of treatment using oral formulation of ibandronate (Bondronat 50 mg).

METHODOLOGY: This is an open-label, one-arm, phase IV study. of the efficacy, safety and pharmacoeconomics of oral Ibandronate (Bondronat) 50 mg in treatment of metastatic bone disease. Efficacy analysis is based on: number of skeletal events assessed by investigator, according to SMPR (Skeletal Morbidity Period Rate), dynamics of biochemical markers of bone destruction, degree and dynamics of bone pain using 5-point scale and analgesic use. Quality of life using SF 36 scale was assessed. Safety analysis includes data for AEs, SAEs, percentage of patients with gastrointestinal intolerability and withdrawn due to intolerance to treatment. Pharma-economic analysis was performed as well.

RESULTS: The total number of treated patients is 47. All patients received at least one dose of Ibandronate (Bondronat 50 mg) and passed at least one evaluation for the efficacy and safety parameters. Totally 37 patients were treated for overall duration of study per protocol.

Dr. Antoaneta Tomova is a specialist in medical oncology from Plovdiv, Bulgaria. She is currently the Head of the First Chemotherapy Department of Plovdiv Complex Oncology Centre. Dr. Tomova has graduated the Medical University in Sofia in 1985. She has dedicated more than 25 years to medical oncology and chemotherapy. Her main areas of expertise are in the fields of medical oncology, palliative care, pain management, and symptom control. Dr. Tomova has attended more than 60 specialized courses abroad so far. She is a member of Bulgarian Cancer Society, BUON, UICC, ESMO and ASCO, where she has presented a poster. She was named Doctor of the Year in 2009 from the National Association of Patient with Oncology Diseases, and was voted The Doctor Whom Patients Trust in 2012. Dr. Tomova speaks 2 foreign languages English and Russian.

PROF. DR. JASMINA MIHAILOVA

ML 18061 – PHASE IV OPEN, PROSPECTIVE, MULTICENTER, NON-COMPARATIVE, NON-RANDOMIZED, BULGARIAN STUDY ON SAFETY AND TOLERABILITY OF ADJUVANT TREATMENT WITH XELODA ® (CAPECITABINE) IN PATIENTS WITH RESECTED COLON CANCER

BACKGROUND: Colorectal cancer is one of the most common malignancies, accounting for about 1,360,000 new cases worldwide every year 1, Patients (pts) with stage I-III colon cancer (CC) are candidates for curative resection. However, more than half the patients with stage III disease who received curative resection eventually develop metastases during the course of their disease 2. For such pts, adjuvant chemotherapy has a role to eradicate micrometastases and then prevent tumor recurrence. The benefits of adjuvant chemotherapy in terms of reducing recurrence and achieving superior disease-free survival (DFS) and overall survival (OS) in pts with resected CC are well established 3-5. As first-line treatment for metastatic CC, capecitabine is an established alternative to the combination of fluorouracil and leucovorin (Fu/L) and is associated with fewer adverse effects than the Mayo Clinic regimen. In the adjuvant setting, the X-ACT trial shows that in CC stage III disease, DFS among pts who received oral Capecitabine is at least equivalent to that among those who receive Fu/L by i.v. bolus 5. The adjuvant capecitabine is at least equivalent to the Mayo Clinic regimen in pts younger than 70 years and those 70 years of age or older. The safety advantage of capecitabine over Fu/L is

maintained in these subgroups 8. Because of the efficacy of capecitabine in metastatic and adjuvant setting in CC pts the further data regarding capecitabine toxicity and tolerability are needed.

OBJECTIVES: The primary endpoint is safety and tolerability of adjuvant therapy with Xeloda ® (Capecitabine) in resected colon cancer patients.

PATIENTS AND METHODS: Pts older than 18 years of age are required to be fully recovered after surgery (at least 4 weeks after operation) for histologically confirmed stage III colon carcinoma. ECOG performance score of 0-2, signed informed consent for the study and laboratory parameters with accepted norms for chemotherapy are required. Pts ineligible for participation : with evidence of metastatic disease, including tumor cells in ascites or microscopic evidence of residual disease; with tumor markers levels (CEA and/or Ca 19-9) after operation > 1.5 ULN; with prior cytotoxic chemotherapy or organ allograft; with clinically significant cardiac disease, severe renal impairment, central nervous system disorders, or psychiatric disease or pregnancy; with serious uncontrolled infection, who are on warfarin or sorivudine therapy, pts with known DPD insufficiency and known allergy to fluoropirimidins. Sexually active premenopausal women and men unwilling to practice contraception were ineligible.Patients are treated 24 weeks with eight cycles of oral capecitabine, at a dose of 1250 mg per square meter of body-surface area, twice daily on days 1 through 14 every 21 days. Adverse effects are recorded at any cycle. The last evaluation is 4 weeks after the last dose of Xeloda® (Capecitabine). The evaluation of safety is done by percentage of pts with adverse reaction and the degree of which; the percentage of pts with unexpected serious adverse reaction; the percentage of pts with dose reduction. The tolerability evaluation is done by percentage of pts who have stopped earlier the planned treatment due to intolerability to Xeloda. Statistical methods are descriptive, Kruskal Wallis test for group comparison and Cox regression analysis for risk factors influence on appearance of adverse reactions.

RESULTS: From August 2005 till March 2007 sixty three pts from six Bulgarian sites are entered. In the study are enrolled patients with mean age of 62.6 years old, among whom the percentage of women are higher in comparison to men.(55% vs 45%). From the 63 studied pts per protocol so called "safety population" 76% (48 pts) are completed the planned treatment. Among pts not completed planned treatment 24%-15 pts) only 6.3 (4 pts) have reasons connected with adverse events. The total number of AE reported are 115, from which 6 (5.2%) are serious. The AE are mostly Grade 1 (51.3%) and Grade 2 (38.3%). The drug-related AE are found in 57 pts (49.6%). The five most frequent AE are hand-foot syndrome (25%), nausea (13%), diarrhea (12%) and hyperbilirubinemia (7%). Data are shown that AE have appeared most often in women (87%) that in man (64%). In addition, among drug-related AEs the stomach pain and nausea are the most frequent AEs in women in comparison to men. The most of the drug-related AE have appeared in the first 110 days of treatment. In addition about 75% of all drug-related AE are lasted for average of 22 days.

CONCLUSIONS: This multicenter study for safety and tolerability of adjuvant treatment with Xeloda® (Capecitabine) in resected colon cancer patients is the largest prospective study which has been conducted in Bulgaria. The study results are revealed good tolerability of Xeloda® based on 76% of patients who completed planned treatment. The recorded AEs are mild and moderate of grade and are resolved without complications. The most frequent AE is hand-and-foot syndrome -25%. Women suffer more frequently from AEs during treatment with Xeloda® than men. Adjuvant treatment with Xeloda® is well tolerated with mild and controlled AEs.

Assoc. Prof. Dr. Jasmina Mihailova is currently the Head of the Medical Oncology Department in the Military Medical Academy in Sofia, Bulgaria. Assoc. Prof. Mihailova graduated in the Medical University in Sofia in 1991 and started working in the Palliative care department of Sofia oncology dispensary, later on moving to the ambulatory chemotherapy department (1994). She specialized in Internal Disease and in Medical Oncology (2002). Later on she acquired the degree of an Assoc. Prof. in Oncology in 2012 and that of a Professor in October 2014. In the period 2002 – 2004, Assoc. Prof. Mihailova has been specializing with ESMO and AUCC grants in the Medical Oncology department of the University Hospital in Perugia, Italy. Her scientific project includes a clinical study design and an assessment of the biologic angiogenesis factors in lung cancer (FABIOLA project).

She has also had several specializations in Leicester and Oxford (UK), as well as in the Clinic of Medical oncology and Radiotherapy of the Rambam Medical center in Haifa, Israel (2009). Since 2004, she has been working in the Clinic of Haematology and Oncology at the Military Medical Academy in Sofia, and since 2008 had been appointed as the Head of the Medical Oncology Department. Assoc. Prof. Jasmina Mihailova is a member of the SEE Lung Working Group and since 2010 has been the Bulgarian national representative for ESMO. Her total individual impact factor is 15 and she has been a co-author in more than 110 articles.

QAISAR SIRAJ, MD, PHD

RADIOLABELED MONOCLONAL ANTIBODIES IN THE TREATMENT OF SOLID TUMOURS

The human body secretes antibodies in response to foreign antigens. This phenomenon manifests itself through the B-cell lineage with help from T-cells and other components of the immune system. A normal humoral immune response results in multiple clonal lineages of B-cells which terminally differentiate into antibody-secreting plasma cells resulting in a polyclonal antibody response. However, for therapeutic use, only a monoclonal antibody (one plasma cell clone) is required. This was first made possible in 1975 through hybridoma technology by the fusion of antibody-secreting plasma cells and immortal murine myeloma cells, with the benefits of each retained. The major drawbacks of purely murine monoclonal antibodies are a reduced plasma half-life compared with human IgG and the production of the human against mouse antibody (HAMA) response, which further reduces the half-life. To overcome this, chimeric, humanized and human MoAbs have now been developed.

Molecular targeting therapy using monoclonal antibodies (MoAbs) has become a relevant therapeutic strategy for cancer with several MoAbs currently being used for the treatment of malignant tumours. The targeting of a cytotoxic radionuclide to a specific cancer cell offers an elegant alternative to conventional forms of therapy. Radiolabeling of MoAbs provides a radioimmunoconjugate composed of an antibody and a radionuclide, which shows the synergistic effect of radiation and immune-mediated cellular toxicity, thereby enabling increased efficacy and minimizing toxicity. Radiolabeled tumor-selective MoAbs have proven to be useful in the localization and assessment of metastatic disease and are emerging as indicators of therapeutic progress. Radioimmunotherapy for haematologic malignancies has shown promising results and currently several radiolabeled MoAbs are being tested for solid tumours.

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

PhD in Nuclear Medicine, 1993
Royal Free Hospital School of Medicine, University of London
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AWARDS & HONOURS

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- Chairman's Award for Excellence, Portsmouth Hospitals NHS Trust, 2005
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- Distinguished Alumnus, Dow Medical University, Karachi, 2004
- Best Poster Award, British Nuclear Medicine Society, 2001

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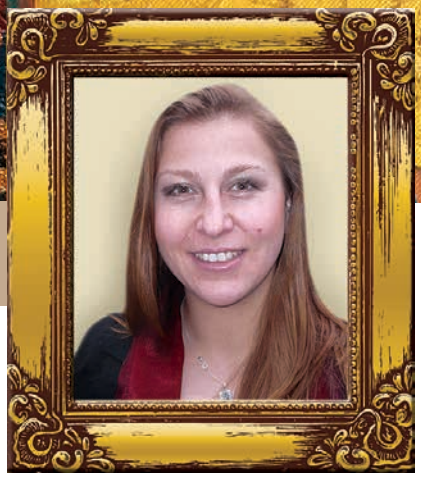

DR. ASSIA KONSOULOVA

Dr. Assia Konsoulova is a medical oncologist in training, working at the Introduction to the Internal Diseases Department in the Medical University in Varna, Bulgaria.

Dr. Konsoulova graduated the Medical University in Varna in 2003 and later specialized in Internal Medicine (2011). She has won internships and attended more than 10 educational courses in Belgium, Italy, Switzerland, Slovenia, Croatia and Germany. She has 14 scientific publications on various topics in oncology and she is currently a member of 4 research projects focusing on the diagnosis and treatment of breast and pulmonary cancer.

Apart from being the responsible for ENTYAC (European network for teenagers and young adults with cancer) and for the European Initiative in Quality Management in Lung Cancer Care for Bulgaria, Dr. Assia Konsoulova is also a member of the National expert council for Medical Oncology at the Health ministry, the ethical committee at the Society of the Young oncologists in Bulgaria, and the Union of the Quality specialists in Bulgaria. She is the founder and a member of the board of the National Scientific Society for Medical Oncology. 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. Assia Konsoulova speaks 4 foreign languages - English, French, Russian and German.

SACHA ROTHSCHILD MD, PHD

THE IMMUNO-ONCOLOGY REVOLUTION: IMMUNE CHECKPOINT INHIBITORS IN THE TREATMENT OF LUNG CANCER

The vast majority of tumors are characterized by high frequencies of genetic and epigenetic alterations resulting in tumor-specific antigens, which may, in principle, be recognized by cytotoxic T-cells. Though early clinical immunotherapy trials have yielded mixed results with ambiguous clinical benefit, cancer immunotherapy is now attracting increasing attention as viable therapeutic option, mainly in melanoma and lung cancer but increasingly also in other malignancies(1–3). In particular, recent therapeutic efforts targeting inhibitory receptors on T cells to overcome tumor-induced immune dysfunction have the potential to reshape current treatment standards in oncology. The clinical development has been pioneered by the antibody ipilimumab, which blocks CTLA-4 and has demonstrated survival benefit in two randomized landmark trials in melanoma(2,4). Capitalizing on this success, the research on the clinical implication of T cell checkpoint inhibition has been boosted. Early clinical trials have demonstrated meaningful response rates, sustained clinical benefits with encouraging survival rates and good tolerability of next-generation checkpoint inhibitors, including PD-1 and PD-L1 inhibitors, across multiple cancer types(5–9). Attractive perspectives include the concurrent blockade of immunologic (nonredun-

dant) checkpoints, which has recently been demonstrated using combinations of immune checkpoint modulators themselves or with other therapies, such as chemotherapy, targeted therapy or radiotherapy(4,10–14). Historically, lung cancer has not been considered sensitive to immune-based therapies and was believed to be a non-immunogenic tumor(15). Most lung cancer patients present with metastatic disease and are immune suppressed with decreased peripheral und tumor lymphocyte counts(16,17). Furthermore, the local tumor microenvironment in lung cancer is highly immunosuppressive(18). Regulatory T cells (Tregs-CD4+) play a key role in the suppression of the tumor immune surveillance by suppressing cytotoxic T lymphocytes (CD8+ T cells). Tregs have been found at higher levels in peripheral blood and tumor environment in patients with lung cancer(19). On the other hand, a high number of tumor-infiltrating Tregs, CD8+ T cells, natural killer cells, and/or dendritic cells have been associated with improved patient survival(20–25). Based on promising results of immunotherapeutic approaches in other solid tumors and the development of new molecules unleashing the immune system, immunotherapy has again raised interest in the treatment of lung cancer. Strategies to actively enhance the immune response in lung cancer includes vaccination to stimulate antibody and T-cell responses to cancer cells and use of immune checkpoint inhibitors to boost T-cell immune responses to lung cancer cells.

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Dr. Sacha Rothschild MD, PhD is a medical oncologist in the Department of Oncology at the University Hospital Basel, Switzerland.

Dr. Rothschild graduated the Literargymnasium Rämibühl, Zurich in 1997, and later on the Medical School of University of Zurich, where he got his Swiss Federal Medical Diploma in 2003. He got his Medical Doctor degree in 2007 with magna cum laude, and later that year he took his Swiss board exam in Internal Medicine (FMH). He also had his European exam in Medical Oncology (ESMO) and his Swiss board exam in Medical Oncology (FMH) in 2009. Two years later in 2011, he acquired a PhD degree from the University of Bern and in 2016 he got his habilitation for Medical Oncology at the University of Basel.

In the period 2012-2015, Dr Sacha Rothschild has won 8 different grants from different cancer research organizations. He also has held a couple of research positions at the University of Bern (2009-2011) and at the University of Cologne (2014-2015), and since 2015 is a Project Leader in the Department of Boimedicine, Cancer Immunology and Biology at the University of Basel.

He has also held a number of clinical positions in Spital Laufenburg, Zurich University Hospital, Kantonsspital Aarau, and Bern University Hospital. Dr. Rothschild works in the Medical Oncology Department in the University Hospital Basel since 2011, where he currently acts as the Head of Network for Molecular Tumor Therapy in the Cancer Center (since 2015), as the Head of Lung Tumor Center (since 2015), and as a Consultant (Leitender Arzt) since 2016.

Dr. Rothschild has published 27 peer reviewed original articles, 22 articles in peer reviewed journals, chapters in 4 books, as well as 6 clinical case reports.

Dr. Sacha Rothschild as a member of a number of scientific societies like FMH, SGMO, ESMO (full member), ASCO (associate member), AACR (associate member), IASLC, ETOP, SAKK, and the Swiss MD-PhD Association. He has participated in more than 50 clinical trials (phase I-IV) as principle investigator and as a sub-investigator at the University Hospitals Zurich, Bern and Basel and the Cantonal Hospital Aarau.

NATALIYA CHILINGIROVA, MD, PHD

THE EVOLVING ROLE OF IMMUNOTHERAPY IN THE TREATMENT OF MALIGNANT MELANOMA

The incidence of malignant melanoma has been steadily increasing in the last 30 years and prognosis for patients was considered to be poor. A truly profound change in recent years is the advent that changed melanoma treatment approach and showed new horizons for potential cancer therapies. These cutting-edge research efforts into targeting key T-cell immune check points led to new novel therapeutics. This is a brief review of the key areas of treatment and research activity in melanoma immunotherapy.

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. SubInvestigator 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. ZAHARII KRASTEV

NON-SPECIFIC CANCER IMMUNOTHERAPY

Cancer is an immune disease. Cancer treatment enhances the present immunosuppression. Surgical trauma, itself, worsens the condition of the immunodeficiency patients, and chemotherapy reduces the production of cytokines.

Few neoplasms that are not susceptible to immunotherapy. The following compounds are considered as immunomodulators In the textbooks of clinical pharmacology - BCG vaccine, thymosin, interferon, interleukin 2 (IL-2) imunotsianin, isoprinosine and levamisole. More than 10 immune products with a specific anticancer effect have been approved over the past 25 years. BCG vaccine is the oldest non-specific immunomodulator with an effect in various neoplasms, including its combined use with chemotherapy in breast cancer. It has been shown that the medication Calgevax corrects the imbalance of T-cells. Levamizol induces T-cell differentiation and has been approved for colon cancer at a dose of 150 mg per day for 3 consecutive days every 2 weeks. IL-2 is a highly effective immunomodulator, particularly if administered into the tumor. The subcutane-

ous administration of low doses of IL-2 prevents from relapse in most neoplasms. Melatonin, dosed at 20-40 mg at night affects the NK-cells, the lymphocytes, and the release of cytokines. Izoprinozine has an antiviral effect in 75% of cases with neoplasms and, if administered during radiotherapy, restores immunity of patients. Retinoids have antiangiogenic effects much like IL-2 and are synergistic with the latter, increasing in multiple times the production of gamma-interferon. Specific examples of the successful application of IL-2 in mesothelioma, liver cancer and cancer of the colon have been presented, and the change in lymphocytes and cytokines in those patients.

Non-specific immunotherapy:

1. Should start from the time of cancer diagnosis – e.g. preoperatively, by suspending antioxidants, because they make cancer cell resistant to radio- and chemotherapy.
2. Can be combined with chemotherapy or radiotherapy
3. Relapse prevention treatment is recommended for at least 3 years
4. It can be applied topically (inside, peritumoral or intravascular) or system-subcutaneous, as scarification, orally.
5. The effect occurs after 3-6 months and unfolds after 9-11 months
6. Some immunomodulators can be administered synergistically: BCG and IL-2; IL-2 and melatonin, IL-2 and 13-cis retinoic acid, levamisole and isoprinosine.
7. Immunotherapy should be avoided when biomarkers suggest negative effect
8. The absolute number of lymphocytes in the periphery is a good marker of effect.

The pressure exerted by relatives and friends of patients plays an essential role in the selection of a "secret" immunotherapy, conducted without medical supervision. Only approved immunomodulators, for which scientific evidence is available, should be used. There is enough evidence about melanoma, urinary bladder cancer, primary liver cancer, colon cancer, breast breast, lung cancer, kidney cancer, and mesothelioma.

It is the right of the patient to receive an approved-for-use immunotherapy.

Prof. Dr. Zaharii Krastev is an imminent Bulgarian specialist in the field of gastroenterology, currently working as a consultant for the Clinic of Gastroenterology in St. Ivan Rilsky University Hospital in Sofia, Bulgaria. Prof. Krastev was born in 1943 in Sofia. He graduated high school in 1961 and later on the Medical University in Sofia as a medical doctor (MD) in 1969. He got his specialty in Internal medicine in 1975 and the one in Gastroenterology in 1978. He also acquired a PhD following his dissertations on dysproteinemia in chronic hepatic diseases (1979) and on the assessment protocols of hepatic impairment (1988). He had a number of specializations abroad including 2 in France and one in Vienna, Austria.

Prof. Krastev has a long carrier having served as Head of Gastroenterology Clinic (1989-2008), Deputy-Head of Sofia Medical Academy (1990-1992), and as a Head of Internal Diseases Clinic (2000-2008). Prof. Krastev is known for 30 years for his participation in a great number of phase II and III major trials in the fields of chronic viral hepatitis, IBD, IBS, and ulcers. He has more than 170 articles in Bulgaria and more than 60 peer reviewed scientific publications abroad, and has been cited on more than 1200 occasions. He has participated in the writing of 15 textbooks (including Internal Medicine Chief Editor, 2005 and 2010). Prof. Krastev has written a monograph on the contemporary treatment of ulcer, and has attended numerous congresses in the field of gastroenterology both in Bulgaria and abroad. He is currently a member of the Editorial boards of Bulgarian Hepato-gastroenerology, Contemporary Medicine and Medical Review, as well as of World Journal of Gastroenterology and Hepato-gastroenterology. Prof. Zaharii Krastev is an Honorary Member of the Bulgarian Society of Gastroenterology and the Bulgarian Association of Surgeons and Gastroenterologists, as well as of the European Association for the Study of the Liver and of the Romanian Association for the Study of the Liver. He has also been a lecturer at the European School of Gastroenterology and various scientific meetings outside Bulgaria. He is the President of St. Nikola foundation and a member of the Management Board of the Bulgarian-Austrian Alma Association, as well as a member of the Hepatitis foundation.

Prof. Krastev is a founder and head of the Bulgarian-German Rotary Committee and of 4 other Rotary clubs in Bulgaria. He has also been a former President of the Sofia club and has taken part in numerous educational programs of Rotary club Bulgaria.

Prof. Zaharii Krastev speaks 4 foreign languages – English, German, French and Russian.

BORIS PETROV, MD

NEW DIAGNOSTIC PARADIGM IN THE CURRENT AND THE FUTURE PERSONALIZED CANCER TREATMENT – A TOUCH OF OVERCOMING THE RESISTANCE TO TREATMENT – CASE REPORTS

It has now been widely demonstrated that cancer is a genetic disease, by the fact that it is mutations in certain genes, i.e. oncogenes and tumour suppressor genes, which cause the disease. Cancer cells contain key genetic differences compared to normal cells in the same patient. These tumour specific differences (also known as somatic mutations) include changes in the genome sequence, changes in the copy number of specific genes, including amplifications and deletions, and rearrangements or joining together of disparate sequences in the genome.

Specific mutations of tumour genes can now be detected and they provide a molecular view of the mechanisms which drive tumour growth. This advancement has stimulated new approaches to personalized cancer treatment.

A key aspect in almost all cancer genome analyses performed to date is that tumours are highly complex. No two tumours are identical and it's impossible to predict which genetic alterations are present in an individual cancer without a direct sequence analysis of the tumour. Genome-wide analyses of the first 100 tumours from cancers of the breast, colon, pancreas, brain and ovaries have shown that many of the identified mutations were novel and could not have been predicted without direct sequencing of the tumour tissue.

The analysis of tumour DNA gives a molecular view of the genetic modifications compared to the DNA in normal cells of the patient. This makes many applications possible, especially.

- Better classification of the cancer
- Help with the choice of targeted therapy
- Prediction of resistance or response to treatment
- Analyses of differentiation of tumour clones
- Monitoring of tumour DNA
- Analysis of metastases

DR. PETYA BALIKOVA

Dr. Petya Balikova is a resident at the department of Medical Oncology in University Hospital "Tsaritsa Yoanna" ISUL – Sofia, Bulgaria. There she works since 2015. She graduated with distinction from "Plovdiv medical university" – Plovdiv, Bulgaria.

She has interests in internal medicine, oncology and oncodermatology.

She is dedicated to her patients and very passionate about doing research work in immunotherapy and targeted therapy as the future of cancer treatment.

GEORGE F. SAMELIS, MD, PHD

TARGETED THERAPIES IN COLORECTAL CANCER ACCORDING TO THE MOLECULAR PROFILE OF THE TUMORS

There remains a high unmet need in the treatment of colorectal cancer (CRC), which was the second leading cause of cancer-related deaths in Europe in 2012, responsible for 215,000 deaths. Approximately 25% of patients with CRC present with metastases at initial diagnosis and almost 50% of patients with CRC will develop metastases. This contributes to the high mortality rates reported for CRC; the 5-year survival rate of patients diagnosed with stage IV mCRC is about 11%.

2013 marks 10 years from the approval of the first targeted agent, bevacizumab, in colorectal cancer. Since the FDA approval of bevacizumab (Avastin®), we have seen the sequential approval of cetuximab (Erbitux®), panitumumab (Vectibix®), ziv-aflibercept (Zaltrap®), and regorafenib (Stivarga®). The approval of these angiogenesis and epidermal growth factor receptor (EGFR) targeting agents has been based on benefits in overall survival in metastatic colorectal cancer patients in the first, second, and chemotherapy-refractory settings.

LONSURF is currently available in Japan for the treatment of unresectable advanced or recurrent CRC and in the United States for the treatment of patients with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy. LONSURF is an oral combination anticancer drug of trifluridine (FTD) and tipiracil (TPI), whose primary mechanism of action differs from fluoropyrimidines.

Since the approval of cetuximab and panitumumab in the metastatic colorectal cancer in 2004 and 2006 respectively, significant progress has been made in defining mechanisms of resistance to anti-EGFR therapy and in improving patient selection. In this issue, Harlaldsdottir and Bekaii-Saab provide a comprehensive review on the role of anti-EGFR therapies in colorectal cancer. Both monoclonal antibodies, when administered as monotherapy, have been associated with favorable outcomes in patients with chemotherapy-refractory KRAS wild type colorectal cancer. Indeed, the OS of patients with chemoresistant disease and KRAS wild type disease is doubled when compared to best supportive care in patients treated with cetuximab monotherapy. Similar advantages in OS are expected from the integration of panitumumab monotherapy. Panitumumab monotherapy has been noted to be equivalent to cetuximab monotherapy in a recent phase III clinical trial (ASPECCT) in patients with KRAS wild-type patients. The estimated hazard ratio on the ASPECCT trial was 0.966 (95% CI: 0.839-1.113) favoring the panitumumab arm.

Both agents have been associated with an improvement in OS in the first line treatment of metastatic colorectal cancer. In an updated analysis of the PRIME study investigating FOLFOX + panitumumab vs. FOLFOX chemotherapy, panitumumab-treated patients with exon 2 KRAS wild type metastatic colorectal cancer experienced a statistically significant 4.4-months improvement in OS (P=0.027) . Similarly, the addition of cetuximab to FOLFIRI has been associated with a statistically significant 3.5-months improvement in OS in the first line setting when limiting the analysis to patients with KRAS wild type metastatic colorectal cancer. Improvements in PFS and RR have also been documented from the integration of cetuximab and panitumumab in the second line treatment of KRAS wild type (panitumumab) metastatic colorectal cancer. However, an improvement in OS from anti-EGFR therapy integration in the second-line therapy has yet to be demonstrated. The lack of an OS benefit could be attributed to cross-over to anti-EGFR therapy in the salvage setting. At this time, the integration of anti-EGFR therapy (cetuximab or panitumumab) can be considered in combination with chemotherapy in the first (panitumumab + FOLFOX, cetuximab + FOLFIRI), second-line (panitumumab + FOLFIRI, cetuximab + irinotecan), or subsequent chemo-resistant settings (panitumumab or cetuximab monotherapy, or cetuximab plus irinotecan). Given the ASPECCT data and the similar improvements with these agents in the first and later settings, it is not unreasonable to use cetuximab or panitumumab interchangeably. In contrast to anti-angiogenesis therapies, there is no supportive data on the continuation of anti-EGFR therapy beyond progression and therefore a re-challenge with these agents is not considered a standard approach at this time.

Despite the improvements in OS in the first line treatment of KRAS wild type patients, there has been limited integration of these agents in the first-line treatment in the US. This is in part related to the associated dermatological toxicities with these agents, especially when used for protracted periods. A comprehensive review on the dermatological toxicities and their management is presented by Urban and Anadakt in this issue.

A better understanding of the mechanisms of resistance to anti-EGFR therapy may help better select for appropriate patients or lead to novel approaches to complement EGFR targeting. In this issue, Shaib et al. detail some of the potential mechanisms of resistance to anti-EGFR therapy. In addition to the markers detailed in the Shaib article, there is an increased interest in non-exon 2 RAS mutations as markers of resistance to anti-EGFR therapy. Indeed, the exclusion of NRAS mutations and non-exon 2 KRAS mutations on the PRIME study has been recently associated with further improvement in OS in the panitumumab arm compared to chemotherapy alone (26 vs. 20.2 months, P=0.043) . The exclusion of NRAS and non-exon 2 KRAS mutations (in addition to exon 2 mutations) has been similarly associated improvements in PFS and OS on the first line PEAK study. A trend to a worsened outcome was noted with the addition of panitumumab on both the PRIME and PEAK study in NRAS and non-exon 2 KRAS mutations, suggesting that this group of patients does not benefit—and may be potentially harmed—from anti-EGFR therapy. Of note, the exclusion of NRAS and non-exon 2 KRAS mutations results in the additional exclusion of approximately 15% of exon 2 KRAS wild-type patients, therefore enriching further for good responders to anti-EGFR therapy. If confirmed across other anti-EGFR studies, these findings may lead to an increased integration of anti-EGFR therapies in the front-line treatment of a molecularly-appropriate patient population.

Do consider cetuximab or panitumumab in the first line treatment (or beyond) of metastatic colorectal cancer, especially when response matters, and only in KRAS wild type patients. Do not integrate biological therapy in the adjuvant or neo-adjuvant treatment of localized or resectable metastatic colorectal cancer. A positive impact on resectability or recurrence has never been documented in those settings.

We can only see further progress from continuing the path towards offering the appropriate medicine to the appropriate patients. Considerable strides have occurred in narrowing the anti-EGFR candidate population. If the "all" RAS mutant population is excluded, we anticipate that only 45% of patients would be eligible for anti-EGFR therapy. Excluding BRAF mutants would identify only a 35% of metastatic colorectal cancer patients with the best potential response to anti-EGFR inhibition. We recognize that the aggregate of these markers requires further retrospective prospective validation across other completed randomized studies; such results would be eagerly awaited. We would hope that similar progress would be made on identifying markers of benefit to anti-angiogenesis therapies. The identification of markers of response and resistance will not only be essential to apply individualized therapies but also to identify novel pathways for drug development in colorectal cancer.

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Dr. Georgios Samelis graduated from the Medical School of the University of Athens in 1980. He received the Internal-Medicine specialty in 1986. He obtained his PhD from the Medical School of the University of Athens in 1996. He then trained in Medical Oncology for three years at University Oncology Hospitals "Free University" in Amsterdam and "Gustave Roussy" in Paris. He obtained the Medical Oncology specialty in 1999.

Dr. Samelis authored, monographically, more than 50 scientific Greek/English international textbooks. He has participated in more than 200 presentations in Greek/International oncology conferences. He has attended more than 200 educational seminars in Greece and abroad. He has authored more than 100 scientific papers in Greek and English scientific journals. Dr. Samelis is a member of more than 15 Greek/International scientific societies (including ASCO, AACR, ESMO, EORTC, NDDO, HeCOG, EOPE, Greek Society of Senology).

He is a former elected member of the Board of Directors (Accountant) of the Greek Society of Medical Oncologists, as well as a former elected general secretary of the Board of Directors of the Greek Society of Senology. He is an elected member, Vice President of the Greek Society of Oral Oncology since 2011. He is elected President of the Hellenic and International Society of Molecular Targeted Personalized Treatments (HISMTPT) since 2013. He is Editor in Chief in the electronic newsletter " Molecular Signature"-within the HISMTPT. He is permanent reviewer of the European Journal of Cancer and other Medical European journals. Dr. Samelis has been a member of the Scientific Committees for various oncology conferences. He was a regular evaluator of Registrars A and B in Medical Oncology for Regional Health Systems (DYPE) A and B in Greek Hospitals in the area of Athens.

Dr. Samelis is working for Hippokrateion General Hospital of Athens since 1990 and holds the position of Director in the Oncology Department.

PROF. JASNA MIHAILOVIC, MD, PHD

^{18}F-FDG PET/CT IN STAGING AND FOLLOW-UP OF PATIENTS WITH COLORECTAL CANCER

Colorectal carcinoma (CRC) accounts for 13% of all malignancies in the Western World Countries (United States and Europe). It presents the third leading cause of cancer-related deaths in the US. In 2008, CRC was the third most common cancer in human population, with approximately 66% of the 5-year survival rate. 18F-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 CRC. 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. In addition, 18F-FDG PET/CT is important in incidental detection of occult primary colonic tumors.

KEY WORDS: 18F-fluorodeoxyglucose, Positron-Emission Tomography; Colorectal Cancer; Staging; Follow-up

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Prof. Jasna Mihailovic, MD, PhD has been employed at the Oncology Institute of Vojvodina in Sremska Kamenica, Serbia, where she works as the Director of the Department of Nuclear Medicine.

Prof. Mihailovic graduated medical school in 1979 and got her specialty in Nuclear medicine in 1993. She also holds a degree in Healthcare management from the University of Belgrade (2008). As a senior research associate she is lecturing, teaching and mentoring at postgraduate studies of the Medical Faculty of the University in Novi Sad. She is also a Professor at the Technical Faculty "Mihajlo Pupin", Zrenjanin, University of Novi Sad.

Prof. Mihailovic has published several monographs in Serbian and one in English and is the author of 10 chapters in books published in Serbia and abroad as well as of 28 full scientific papers in national and international journals. She has won several awards and a considerable number of fellowship grants in her country and abroad. She has also participated in several research projects some of which she has instituted. Further to that prof. Mihailovic has organized several accredited professional courses and international symposia and has been invited as a lecturer in more than 40 scientific events, including 13 occasions as Chairperson. During her professional career, she has studied molecular imaging in the leading institutions in the world and more recently in the United States.

Prof. Jasna Mihailovic has been a member of 5 scientific committees and a President of the Organizing Committee of 4 international meetings. She is also a Member of the Editorial Board of 5 specialized medical journals like the International Journal of Radiology and the European Journal of Nuclear Medicine and Molecular Imaging.

PROF. GEORGE ZOGRAFOS, MD, PHD

SURGERY FOR COLORECTAL CANCER – NEW METHODS COMPARED WITH THE OLD CLASSIC OPERATIONS

The indications for minimally invasive surgery techniques have progressively been expanded to include colorectal cancer treatment. Tangible evidence of oncologic safety was demonstrated, and long-term results of new minimally invasive techniques have been found comparable to those of open surgery. These new methods provide short-term superiority, less surgical injury, lower immune function depression and better postoperative outcome;they are particularly suitable for delicate and difficult patients, such as elderly or obese.On the contrary, the lower costs have led to still consider open surgery as a valid alternative for low-impact resections (such as right colectomy).

The continuous development in the field of minimally invasive surgery has recently led to the introduction of the single-incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery (NOTES) techniques, which allow better aesthetic results, even if their validation has not yet reached scientific evidence.Prolonged operating time, increased costs and learning curve are the major drawbacks of minimally invasive methods for colon cancer.

Furthermore, robotic surgery is an emerging field in colorectalsurgery and may overcome the limitations of conventional laparoscopic surgery, such as rigid instrumentation, poor ergonomics, and assistant-dependent camera movements and retraction. However, it is still in its earliest steps and limited long-term outcomes data is available.

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 (19830, 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 99mTcO4Na 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 Insitute 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.

FLORA ZAGOURI, MD

ADJUVANT CHEMOTHERAPY FOR COLORECTAL CANCER – NEW ASPECTS

Colorectal cancer is the third most common tumor in men and the second in women, accounting for 10% of all tumor types worldwide. For stage I (T1-2 N0 M0), no adjuvant chemotherapy is recommended. For stage II (T3 N0 M0, T4 a-b N0 M0) adjuvant therapy should not be routinely recommended for unselected patients; however, in high-risk patients (lymph nodes sampling <12; poorly differentiated tumor; vascular or lymphatic or perineural invasion; tumor presentation with obstruction or tumor perforation and pT4 stage, MSI), adjuvant therapy could be considered in clinical practice. For stage III (any T, N1-N2, M0), the standard treatment is a doublet schedule with oxaliplatin and a fluoropyrimidine. Although all three combination regimens are superior to 5-FU/FA alone, FOLFOX4 or XELOX should be preferred to FLOX. When oxaliplatin is contraindicated, monotherapy with infusional or oral fluoropyrimidines should be preferred to bolus 5-FU FU/LV. The benefit of combinations with oxaliplatin has been demonstrated in three landmark trials (the MOSAIC study; the NSABP C-07 trial; the XELOXA international phase III study). As capecitabine does not require a central venous access, it may be preferred in many patients. Negative trials (i.e, the CALGB-89803 trial) are related to irinotecan in combination with 5-FU (bolus or infusional). Moreover, there is currently no role for targeted agents associated with chemotherapy in the adjuvant setting for colon cancer. All trials evaluating bevacizumab (NSABP C-08, AVANT) or cetuximab (NCCTG NO147, PETACC-8) are negative.

Dr. Flora Zagouri is a medical oncologist at Alexandra Hospital, Department of Clinical and Therapeutics, University of Athens, Greece.

Dr. Zagouri graduated the Greek-French High school Jeanne d' Arc in 1996, and later the Medical School of University of Athens, where she got her Medical Degree in 2003. In 2008, after 3 years residency in Internal medicine, she started a residency in Medical Oncology and finished her specialization in 2011. Meanwhile, in 2010, she got a Doctorate degree in Medicine with a work on the topic of evaluation of molecular markers in patients with pre-invasive breast lesions excised via vacuum-assisted breast biopsy. In the period 2011-2013, Dr. Zagouri has been a research-clinical breast fellow at the comprehensive Cancer Center Vienna/ AKH, Medical School, University of Vienna, Austria.

Apart from being three-time winner of chess tournaments, and further to winning several state excellence certificates and scholarships, Dr. Zagouri has been awarded best poster at the 34th Annual Pan-Hellenic Medical Conference, Athens (2008), and at the 8th Congress on Women's Health and diseases, Kos island, Greece (2011), as well as an award (2010) and a fellowship (2011) from the Hellenic Cooperative Oncology Group.

Dr. Zagouri has 157 papers published in journals, cited in PubMed, 4 not cited, 61 oral presentations at international congresses and 62 at local congresses (16 of them cited in PubMed), 5 papers published in local journals, 39 round table presentations/discussions at local congresses and 9 at international ones. She has been a part of the Organizing Committees of 8 Congresses and has participated in 10 clinical trials.

Dr. Flora Zagouri speaks English and French as foreign languages.

PROF. GALINA KURTEVA, MD, PHD

Prof. Galina Kurteva studied medicine in the Medical University of Sofia, Bulgaria. She has specialties in Internal medicine and Oncology.

Prof. Kurteva began her career as a resident in the Department of chemotherapy in the Oncology center in Vratsa, Bulgaria (1981-1984). Later on she continued working as an oncologist in the Clinic of Internal medicine at the Institute for Foreign citizens in Sofia (1984-1985). She currently works in the National Oncology Hospital in Sofia, where she started her academic career first as an assistant professor and later on as a senior assistant professor and an associate professor in Medical oncology. She has had specializations in Russia and England.

Prof. Galina Kurteva has been the Head of the Medical oncology clinic since 2011. She has also serves as the National consultant in medical oncology in the period 2012-2014. Dr. Kurteva is a Professor of medical oncology and a leading expert in the field of colorectal cancer, a lecturer and a mentor to students and residents. She is an author of more than 60 articles, abstracts, monographs and educational books. She is also a co-author of the Bulgarian Guidelines for the treatment of solid tumors.

Prof. Kurteva has been a principle investigator in more than 40 international phase II and III clinical trials. She is a member of the Academic board for postgraduate education in oncology, a co-author of educational programs for physicians and nurses, a member and a chairman of the Examination Board for Medical Oncology in Bulgaria. She is also a mentor of residents, who have successfully achieved academic degrees. Prof. Kurteva is an organizer of CME meetings and international courses for students and residents in oncology in Bulgaria.

Prof. Galina Kurteva is a member of the Bulgarian Association for Clinical Trials, Bulgarian Oncology Scientific Society, ASCO (American Society of Clinical Oncology), ESMO (European Society for Medical Oncology), BUON (Balkan Union of Oncology); a member of the editorial board of MEMO (Magazine of European Medical Oncology), the chairman and co-founder of the Bulgarian Educational Oncology Academy.

PROF. UMBERTO RICARDI, MD

STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) IN OLIGOMETASTATIC DISEASE FROM CRC

Colorectal cancer (CRC) is one of the tumors that most often present oligometastatic spread (synchronous oligometastatic, oligorecurrent or oligoprogressive disease), most commonly in the liver and lung. 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. Determining the advantages or the possible superiority of aggressive approach in comparison with systemic therapy alone or observation is challenging because of the predominantly retrospective nature of existing data, which has raised substantial concerns for selection biases (performance status, disease-free interval, small metastatic burden). New alternative therapeutic options such as Stereotactic Ablative Radiotherapy (SABR) or Radiofrequency Ablation (RFA) are increasingly being proposed, combining the ablative effects with a very favorable toxicity profile . Schlijper et al reviewed the clinical reports published until 2011 on the application of surgery, radio-frequency ablation (RFA) or SBRT in patients with pulmonary oligometastases from CRC, selected by a minimum follow-up of 24 months and

a minimum of 50 patients included. Twenty-three surgical series fulfilled the selection criteria, 4 of which were prospective. Survival rates for surgery were 64-88% at 2 years and 29-71.2% at 5 years. Limited data were available for RFA, with survival rates ranging from 64 to 73% at 2 years and 34.9 to 45% at 5 years. No studies on SBRT fulfilled the selection criteria.

SBRT was investigated mainly in the treatment of liver and lung metastases, with promising results and good safety profile, using either a single dose or a small number of fractions, in studies unrestricted to CRC patients. Few studies specifically addressed the role of SABR in patients affected with lung metastases from CRC, with promising results in terms of tumor control probability and safety.

As for other oligometastatic scenarios, there is a lack of prospective controlled data comparing surgery or stereotactic radiotherapy versus observation or systemic therapy alone. The ongoing PulMICC trial (UK, clinicaltrials.gov identifier NCT01106261) is an example of a feasibility study with the aim to determine whether it will be possible to recruit sufficient patients for a larger phase III randomized trial powered to detect statistical differences in overall survival between metastasectomy and active monitoring. This trial is completing patients' recruitment, and will hopefully give us important information not only on clinical endpoints (OS is the secondary endpoint), but also on which patients are routinely offered surgery. The ORCHESTRA trial (A Randomized Multicenter Clinical Trial for Patients with Multi-Organ Colorectal Cancer Metastases Comparing the Combination of Chemotherapy and Maximal Tumor Debulking versus Chemotherapy Alone, NCT 01792934) will also hopefully provide convincing clinical evidence.

Dr. Ricardi is currently Full Professor and Chairman of Radiation Oncology at University of Turin, Italy.

Dr. Ricardi's main areas of clinical and scientific interest include lymphoma, lung cancer, CNS tumors. He is also an expert in the development of cutting edge technologies in Radiation Oncology.

Dr. Ricardi has authored more than 150 full research papers, and participated as invited speaker in a number of national and international conferences. He is active in many educational activities, both at national and international level.

Dr. Ricardi is member of numerous national and international scientific societies. He is deeply involved in the European Society for Radiation and Oncology [ESTRO] (Board of Directors from 2004 to 2006; Executive Administrator from 2006 to 2011; now Chair of ESTRO National Societies Committee). Dr. Ricardi is member of the Steering Committee of ILROG (International Lymphoma Radiation Oncology Group).Dr. Ricardi is member of ART (Advanced RadioTherapy) Committee of IASLC (International Association Study Lung Cancer).

DR. PAOLO CASTELLUCCI

RADIONUCLIDE THERAPY FOR LIVER METASTASES FROM COLORECTAL CANCER

Liver is the most frequent site of metastases in patients with colorectal cancer. New chemotherapies and improvement in surgical techniques allow treating surgically even patients with advanced stages. Radio-embolization using yttrium-90 (90Y) resin or glass-microspheres, selective internal radiation therapy (SIRT), is a pal-

liative treatment which is aimed to reduce the tumor mass and eventually allows surgical resection.

Pre and post treatment evaluation of patients with liver lesions from colorectal cancer are routinely performed with c.e. CT, MRI and c.e.US. Angiography is of key importance since it allows the evaluation of vascular anatomy of the liver before SIRT. SPECT with 99mTc albumin aggregated (99mTc-MAA) is particularly useful to exclude the presence of hepatic shunts to other organs (mainly lungs) before and/or after SIRT.

Several studies have shown the potential role of whole-body 18F-FDG-PET/CT in patients with liver lesions from colorectal cancer undergoing SIRT. 18F-FDG-PET/CT seems to be useful in assessing treatment response; it may have a role in treatment planning and patient selection; it may provide prognostic information. The aim of the oral presentation is to present the experience of our Centre and provide a review of the literature on this topic.

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Policlinico S.Orsola – Malpighi, Via Massarenti 9, 40138 Bologna Italy.
Academic titles: School of Medicine at the Università degli Studi di Bologna, graduation in Medicine and Surgery 12/03/94 with points 110/110 cum laude.
School of Medicine at the Università degli Studi di Bologna, Residency in Nuclear Medicine 02/11/1999 with points 70/70 cum laude.
School of Medicine at the Università Modena e Reggio: Residency in Medical Radiology 28/02/2013 with points 106/110.
Work experience
December 2002 - present: Dirigente Medico di I livello (registrar) at the Servizio di Medicina Nucleare e Centro PET della Azienda Univeristario Ospedaliera S.Orsola –Malpighi di Bologna. From 2005 Professor at the "Scuola di specializzaizone in medicina nucleare", at the University of Bologna.
March 2001 - December 2002: Dirigente Medico di I livello (registrar) at the Servizio di Medicina Nucleare dell'Ospedale S. Croce e Carle di Cuneo; clinical applications of PET in oncology and cardiology.
November - December 2001: Visiting fellow at the CETIR PET center Barcelona, Spain clinical application of PET in oncology and cardiology (Director Prof. Ignasi Carrió).
January - December 2000: Research fellow at the "Istituto Europeo di Oncologia" (I.E.O.) experience on Radio Target Therapy with 90Y and somatostatin analog (DOTA-TOC) and radioguided surgery (ROLL; SNB) (Director, Dr. Giovanni Paganelli).
June - December 1998: fellow at the Department of Radiology, Service of Nuclear Medicine and PET Center, Hospital of the University of Pennsylvania, Philadelphia (Director, Prof. Abass Alavi).
Skillness: Large experience in whole body PET/CT scan reading using 18F-FDG, 11C-Choline, 11C-Methionine, 11C-Acetate, 68Ga-DOTA-NOC, 18F-DOPA, 11C-Ephedrine, 64Cu-ATSM. The PET centre at the Azienda Ospedaliera S.Orsola–Malpighi, Bologna is provided with 3 PET/CT scanners and the output is about 7000-8000 scans per year.
Brain PET scans in oncology (11C Methionine) or brain disorders (18F-FDG). Large experience in organizing a PET centre.
Experience in Radio Target Therapy with somatostatin analog (90Y-dota-TOC). Experience radio guided surgery (sentinel node detection in breast, melanoma, genito-urinary tract and ROLL).
Italian referent for H10 EORTC protocol on the application of PET in Hodgkin Lymphoma.
Member of the EANM group about the application of Choline PET in prostate cancer.
Languages
English: good knowledge of written and spoken language; Portuguese (Brazilian): excellent knowledge of the spoken language; Spanish: fair knowledge of the spoken language.
Publications: Authors and Co-Authors of more than 100 full papers publications in the field of Oncological applications of PET.

ASSOC. PROF. DR. SONYA SERGIEVA

SPECT-CT SOMATOSTATIN-RECEPTOR SCINTIGRAPHY IN COLORECTAL NETS

S. Sergieva, A. Fakirova*, B. Robev, R. Krasteva, M. Dimcheva, A. Jovanovska, Sofia Cancer Center,
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The incidence of carcinoid is characterized with a consistent trend growth also due to the improved diagnosis of these tumors in recent years. The clinical presentation of the neuroendocrine tumors (NETs) may vary depending on the site of tumor origin. About 72% of NETs arise in the gastrointestinal tract. Carcinoid tumors are most commonly found in the gastrointestinal tract and are located in decreasing order of frequency in appendix, ileum, rectum, stomach, and colon.

Carcinoid tumors of the colon are extremely rare tumors, comprising < 11% of all carcinoid tumors and only 1% of the colonic neoplasms. Typically, carcinoid tumors of the colon present in the sixth to seventh decade of life during evaluation for anorexia, abdominal pain, and unintentional weight loss. Data from several series demonstrate that colonic carcinoids tumors are diagnosed usually late in the course of the disease, and the average size of these tumors was approximately 5 cm at diagnosis. Additionally, at diagnosis, approximately two-thirds of patients have local nodal or distant metastases, resulting in an overall 5-year survival rate of 25% to 41%. Rectal carcinoids are usually asymptomatic and are discovered incidentally during proctoscopy, sigmoidoscopy, or digital rectal examination. Patients, who do have symptoms, typically present with rectal pain, bleeding, or constipation. Though these neoplasms represent only 1.3% of all rectal tumors, the true incidence of rectal carcinoids appears to be on the rise due to recent advances in endoscopic technology. Like carcinoids of the small bowel and colon, these tumors are thought to arise from the epithelial endocrine cells; however, unlike these neoplasms, rectal carcinoids contain glucagon and glicentin-related peptides, rather than serotonin. The development of the typical carcinoid syndrome is rare. Interestingly, the size of rectal carcinoids correlates closely with the aggressiveness of the tumor and its metastatic potential. Recent series have shown that tumors smaller than 1 cm rarely metastasize, while lymph node and liver metastases are seen in up to 70% of cases in which the primary tumor exceeds 2 cm. Overall 5-year survival rates from the SEER database for localized, regional, or distant disease spread beyond the rectum and rectosigmoid junction over a ten year period were 90, 49, and 26%, respectively. Patients with suspected NETs should undergo biochemical screening. The most commonly employed marker in patients suspected of having a carcinoid tumor is the urinary 5-hydroxyindole acetic acid (5-HIAA), although the specificity of this marker is only about 88%, and thus elevated 5-HIAA is not necessarily diagnostic. However, 5-HIAA assays have the benefit of being widely available. Chromogranin A may be the best overall marker of NETs and is often elevated as much as 50 to 100% above normal in patients with these neoplasms. A high incidence and density of somatostatin receptors (SSTR2, SSTR3, and SSTR5) are found in colorectal NETs. They have a high affinity for the commercially available synthetic octapeptide octreotide for diagnosis and therapy. Recently, new imaging technique SPECT-CT somatostain-receptor scintigrapy with 99mTc-Tektrotyd have become performed in NETs. Fusion images improve anatomical localization and provide differential diagnosis of the most uncertain scintigraphic lesions, reducing false positive results and thus improving specificity and accuracy of SPECT studies especially in the region below the diaphragm. It can be summarized that main indications for SPECT-CT somatostatin-scintigraphy are as follows:

I. Diagnosis of primary NETs:

1. Limited role only in selected cases to depict the most appropriate tumor lesion for correct biopsy
2. To image primary tumor in cases with metastatic lesions from tumors with unknown primary origin.
3. To assess SSTR expression in order to predict an individual response to therapy and thus could effectively influence the management of individuals with NETs.

II. Staging of NETs: for pre-treatment correct N and M-staging according to the TNM classification.

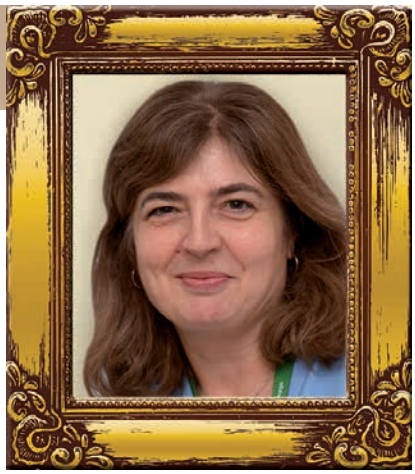
III. Follow-up of patients after therapy

1. Monitoring of treatment response – complete, partial, stable and progressive disease.
1. For differential diagnosis of proliferative tumor tissue from fibrosis in residual tumor masses after treatment.
2. For early determination of recurrence in cases with negative anatomical imaging (CT, MRT) but with clinical and biochemical indices for presence of NETs.
3. For precise topography of metastatic foci in patients with disease extension.
4. In patients with poorly differentiated NETs and negative somatostatin-receptor scintigraphy, PET-CT studies should be performed.

In conclusion, a SPECT-CT study is a potential new technique for staging and follow-up of patients with colorectal NETs in future years.

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

DR. ANELIYA DECHEVA, MD



MICROBIOTA, INFLAMATION AND GASTROINTESTINAL TUMORS

The role of normal or altered flora in intestinal neoplastic process is not entirely clear, but it is assumed that the close relationship between bacteria and chronic inflammation may synergistically potentiate their action in promoting mucosal damage. Clinical and experimental evidences showed that chronic inflammation increases the risk of neoplastic transformation.It is known that proteins of bacterial origin are able to up-regulate the production of COX2 and promote cell proliferation through activation of mitogen-agtivated protein kinase,which increase the incidence of cell transformation and the rate of acquired gene mutations. Subject identification with a "carcinogenic" flora should lead to the change of this predisposing factor through diet, use of prebiotics, probiotics and antibiotics that could reduce the GI cancer occurrence.

Dr. Aneliya Decheva is a specialist in the field of gastroenterology, currently working at Tokuda Hospital in Sofia, Bulgaria.

Dr. Decheva graduated the Medical University in Stara Zagora, Bulgaria, as a medical doctor (MD) in 1996. Later on she got her specialty in Internal medicine in 1999 and the one in Gastroenterology in 2006, both at Sofia Medical University. She has had numerous specializations in Bulgaria and abroad, including 3 in the Netherlands, a couple of ones in the Check Republic, one in Turin, one in Stockholm, and 2 in Germany (Berlin and Heidelberg). Dr. Aneliya Decheva professional experience includes working in the Department of Gastroenterology at Multi-Profile Hospital for Active Treatment Dr. Atanas Dafovski, Kardjali (1992-2006), the Gastroenterology Department in the 5th City Hospital, Sofia (2006-2009), and at Tokuda Hospital in Sofia (2009 – till now). Her major scientific interests are in the fields of hepatology, ultrasound-interventional procedures and ERCP. Dr. Decheva is a member of a number of scientific societies like EASL, BAUM -Bulgarian Association of Ultrasound in Medicine, EFSUMB, BSGGEAU - Bulgarian Society of Gastroenterology, with Affiliated Sections of Gastrointestinal Endoscopy and Abdominal Ultrasound, BASGO-Bulgarian Association of Surgeons and Gastroenterologists and Oncologists.

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