

# 25<sup>TH</sup> HELLENIC CONFERENCE OF CLINICAL ONCOLOGY



# RESPONSE ASSOCIATED TO TOXICITY OF IMMUNOTHERAPY IN PATIENTS WITH METASTATIC MELANOMA

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**Introduction:** immunotherapy represents a major step in the treatment of melanoma, since it changes responses to treatment and overall survival of patients in a dramatic way. However, immunotherapy can be associated with severe, sometimes lifethreatening, toxicity.

**Aim:** the aim of the study was to detect association between toxicity and response to immunotherapy in patients with metastatic melanoma (MM).

**Methods:** a total of 153 MM cases were evaluated during an 8 year period (2011- 2018); 53 were male. The patients' mean age was 44 years (19-90). Evaluation included 79 cases of skin melanoma (76 %), 15 mucosal (14%), 5 ocular (4.5%) and 1 of the brain. Toxicity of immunotherapy has been recorded and evaluated and consequently has been associated with response to treatment.

**Results:** grade 2- 3 toxicity has been observed in 10 cases out of the 27 receiving Nivolumab. In particular, 4 (33%) developed toxicity of the thyroid gland, 2 of the pituitary (16%), 2 transaminemia (16%), 1 adrenal toxicity (8%) and 1 arthritis (8%). Similarly, 14 out of the 41 receiving Pembrolizumab developed toxicity: 4 colitis (10%), 2 thyroid toxicity (5%), 2 transaminemia (5%), 2 pneumonitis (5%), 1 pituitary toxicity (2%), 1 myelotoxicity(2%), 1 myasthenia(2%) and 1 renal insufficiency (2%). Among the 56 cases receiving Ipilimumab 9 developed toxicity: 4 (8%) colitis, 2 (4%) pituitary toxicity, 1 bowel perforation, 1 transaminemia and 1 skin rash. Among the 11 receiving the Ipilimumab/ Nivolumab combination 8 developed toxicity: 3 transaminemia (27%), 4 colitis (36%) and 1 skin toxicity (9%). In total, among the 135 cases receiving immunotherapy, 40 developed grade 3-4 toxicities (30%), while among them response was observed in 27 (68%). On the other hand, among the 95 cases with grade 0, 1 or 2 toxicities, response was observed in 36 (38%). Response was significantly higher among those who developed grade 3-4 toxicity (p:0.003).

**Conclusions:** immunotherapy may cause severe toxicity, however in the present population with MM, has been associated with significant response.

# PROGNOSTIC SIGNIFICANCE OF DISTANT METASTASIS FREE- INTERVAL IN PATIENTS WITH RELAPSED MELANOMA TREATED WITH BRAF WITH OR WITHOUT MEK INHIBITORS

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**Introduction:** melanoma has a rapidly increasing incidence and mortality rate globally. The evolution of novel targeted therapies represents a breakthrough in the history of melanoma treatment. Identifying the prognostic factors associated with long-term response and survival is of crucial clinical significance to optimize patient management. Most of these data have been derived from large cohorts. Systemic therapies might have negated the prognostic effect of baseline factors, such as disease free interval (DFI).

**Aim:** this retrospective cohort study assessed the prognostic significance of distant metastasis-free interval (DMFI) in patients with relapsed BRAF-mutant melanoma treated with BRAF with or without MEK inhibitors (BRAFi±MEKi).

**Methods:** patients with a DMFI of up to 24 months were compared with those with DMFI of more than 24 months, with regard to their postrelapse progression-free survival (PR-PFS) and overall survival (PR-OS).

**Results:** in total, 109 patients were included in the study. Median DMFI was 25.3 (range: 3.4-188.2) months. Median PR-PFS in patients with DMFI of more than 24 months was 7.9 months [95% confidence interval (CI): 6.2-9.7] compared with 5.4 (95% CI: 4.2-6.7) months of those with shorter DMFI (P=0.016). Median PR-OS was 15.6 months (95% CI: 13.6-17.6) in patients with DMFI of more than 24 months and 12.0 months (95% CI: 9.0-15.0) with DMFI of up to 24 months (P=0.289). Multivariate Cox regression analysis showed that DMFI was independently and strongly associated with improved PR-PFS (adjusted hazard ratio=3.21, 95% CI: 1.78-5.77, ≤24 vs. >24 months) and longer PR-OS (adjusted hazard ratio: 2.09, 95% CI: 1.15-3.80, ≤24 vs. >24 months).

**Conclusions:** the present cohort study is one of the first to confirm the association of DMFI of more than 24 months with an indolent disease course, as shown by longer PR-PFS and PR-OS, in patients with relapsed stage IV melanoma treated by BRAF inhibitor/MEK inhibitor.

# LONG SURVIVAL OF AN ELDER PATIENT WITH STAGE IV EGFR (-) AND ALK (-) LUNG ADENOCARCINOMA: A CASE REPORT

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<b>Introduction:</b>	Lung cancer is a leading cause of death from cancer, with a five-year survival rate of 17% for all stages and mean survival of 4-6 months for stage IV disease if untreated and 6-12 months with previous treatments. However, survival seems to be continually improving due to molecular targeting drugs and immunotherapy. We report a case of an 81-year-old male with a 2years survival from diagnosis with Stage IV epidermal growth factor receptor (EGFR) - negative, anaplastic lymphoma kinase (ALK) mutation-negative adenocarcinoma of the lung, with a long survival using 1 <sup>st</sup> line standard chemotherapy and chemotherapy plus a VEGFR inhibitor in 2nd line.
<b>AIM:</b>	Given that stage IV lung cancer portends a poor prognosis, it is feasible in elder patients using standard chemotherapy and cutting edge patient-specific drugs to achieve acceptable quality of life and prolonged survival.
<b>Methods:</b>	An 81-year-old patient was admitted to the day clinic referred from a private physician for assessment and treatment. An abnormal finding on PET/CT scan was present; the latter was performed on a routine basis after a Dermatomyositis/Polymyositis recent diagnosis. The Endobronchial Ultrasound Bronchoscopy (EBUS) revealed a low grade NSCLC (adenocarcinoma). Immunohistochemistry showed TTF1 (+), NapsinA (+) and P63 (-). Moreover EGFR mutations and ALK rearrangement were not detected while PDL-1 was positive at 25%. Smoking history of >60PY, moderate alcohol use, hyperthyroidism and hypertension were reported. computed tomography (CT) scan of the chest revealed locally advanced disease involving the upper lobe and hilum of the left lung. The primary lesion measured 4,3x5 cm while enlarged mediastinal and hilar lymph nodes (LN) 1.5-2.5cm, as well as contralateral supraclavicular LN (2 cm) were present. The upper and lower abdomen and brain imaging revealed no other metastasis. The patient was Stage IV (M1b). Karnofsky performance status (KPS) was 0. A combination of Carboplatin (AUC 5) and Pemetrexed (500mg/m <sup>2</sup> ) q3W was administered for six cycles, followed by Pemetrexed (500mg/m <sup>2</sup> ) q3W as maintenance. Imaging performed 9 months later revealed stability overall although progression in the. The liver lesions were too small (MD=1cm) to perform a new biopsy. Notably the DM/PM symptoms retreated significantly suggesting a paraneoplastic origin while PS remained 0. We decided therefore to start 2nd line treatment with Docetaxel (75mg/m <sup>2</sup> ) q3W combined with Nintedanib 200mg bid P.O. Chemotherapy was administered for 6 cycles and was discontinued due to worsening tolerance and PS (1). However Nintedanib 200mg bid P.O. was continued as maintenance for another 17 months so far.
<b>Results:</b>	Overall, 26 months from diagnosis and start of therapy and 18 months on 2nd line therapy the patient remains alive and progression free with manageable side effects.
<b>Conclusions:</b>	A good prognostic factors can be predictive of survival in patients with non-small cell lung cancer (NSCLC). Good prognostic factors include early stage at diagnosis, good PS, no significant weight loss and the absence of a driver mutation. In the first line of treatment, combination of cytotoxic chemotherapy with a platinum-based doublet remains the backbone of the initial systemic treatment for patients with advanced NSCLC. To our knowledge, there is no sufficient data about immunotherapy administration in DM/PM; although in the patient of this report DM/PM was paraneoplastic, immunotherapy could be detrimental. Given the association of the later with autoimmunity disorders the patient continued 2nd line therapy with Docetaxel / Nintedanib followed by Nintedanib maintenance while immunotherapy will be considered as 3rd line option. Stage IV lung cancer portends a poor prognosis. The long termed survival associated with acceptable quality of life - in the patient of this report - suggest that better outcomes are feasible in some patients using combinations of standard cytotoxic drugs and modern targeted drugs irrespective of patient age and comorbidities.

# HDAC-1, -2, -4 AND -6 EXPRESSION IN SALIVARY GLAND TUMOURS: CLINICOPATHOLOGICAL CORRELATIONS

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**Introduction:** Histone Deacetylases (HDACs), through post-translational histone modifications and subsequent gene expression alterations, are thought to play a key role in carcinogenesis.

**Aim:** To investigate -for the first time to our knowledge- the expression of HDACs in salivary gland tumours (SGTs) and their potential use as diagnostic or prognostic biomarkers.

**Methods:** HDAC-1, -2, -4 and -6 expression (positivity, intensity of staining and H-score) was assessed immunohistochemically in 58 SGT tissue specimens (36 benign and 22 malignant) and was statistically correlated with the clinicopathological characteristics for all cases and patients' survival for malignant SGTs.

**Results:** HDAC-2 positivity was significantly associated with longer overall survival (OS) of patients with malignant SGT ( $p = 0.028$ ). HDAC-2 positivity and absence of HDAC-6 expression were associated with prolonged OS of patients with high-grade malignant SGT ( $p = 0.003$  and  $p = 0.043$ , respectively). Although HDAC-1, -2, -4 and -6 expression is not different between benign, low grade (LG) malignant and high grade (HG) malignant SGTs, enhanced HDAC-2 and HDAC-6 intensity of staining was noted in HG malignant compared to LG malignant and benign SGTs ( $p = 0.017$  and  $p = 0.028$ , respectively). Additionally, high HDAC-2 H-score was significantly associated with longer OS for HG malignant SGT patients ( $p = 0.027$ ).

**Conclusions:** HDAC-2 expression emerges as an important positive prognostic factor, whereas HDAC-6 expression appear to be an adverse prognosis indicator for malignant SGT patients.

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# TUMOR Dx: THE MOST DETAILED MOLECULAR ONCOLOGY PROFILE - APPLICATION TO SOLID TUMORS (FFPE & LIQUID BIOPSY)

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Tumor Dx is the most detailed molecular tool to aid clinical oncologists as it includes: a) Detection of both somatic and germline (inherited) mutations in 632 genes, associated with the appearance of solid tumors and drug response, b) TMB (Tumor Mutation Burden) score associated with the response to immunotherapy and, c) level of Microsatellite Instability (MSI). Mutations include SNPs (Single Nucleotide Polymorphisms), small insertions/deletions (indels), large insertions/deletions (Copy Number variations, CNVs) and selected fusions (ALK, VBRaf, FGFR, NRG1, NTRK, RET and ROS1 fusions). It is conducted using NGS technology and it can be applied in all solid tumors such as breast, lung and pancreatic cancer. To perform Tumor Dx, one FFPE block is required (representative of the tumor) and whole blood from the patient. It can also be applied in the context of liquid biopsy in cases that obtaining solid biopsy material is not an option or the tissue sample is insufficient for the procedure of molecular profiling. bTMB score (liquid biopsy) is derived using a specialized algorithm and appears to correlate with the response to immunotherapy, according to recent studies (PMID: 28972084) and preliminary results of clinical trials (NCT03178552, NCT02848651). It also seems that MSI and TMB biomarkers are independent; colorectal tumors with high levels of microsatellite instability may have low TMB and thus “poor” response to immunotherapy (low PFS). Some cases of Tumor Dx application from our laboratory: a) pancreatic cancer: two clinically significant mutations in KRAS and TP53 were detected (two of the four basic genes in the development of pancreatic cancer) and TMB score 4.9 Muts/Mb, b) non-small cell lung cancer: simultaneous presence of two pathogenic mutations p.Thr790Met (resistant) and p.Leu858Arg (actionable); p.Thr790Met seems to be quite common in the context of EGFR positive mutations.

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# EGFR MUTATIONS IN PATIENTS WITH NON-SMALL-CELL LUNG CANCER (NSCLC) IN CRETE: DATABASE ARIADNE (2005-2016)

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<b>Aim:</b>	Taking into account the limited data regarding the frequency of EGFR mutations in patients with NSCLC in Greece, we aimed to investigate the EGFR status of the patients included in the ARIADNE database.
<b>Methods and patients:</b>	Herein, we present data regarding the prevalence of EGFR mutations from ARIADNE database that included over 1500 patients with NSCLC treated in Crete from 2005 until 2016. The frequency of uncommon, non-classic, EGFR mutations will also be presented.
<b>Results:</b>	570 tumor samples from patients with NSCLC were tested (570/1555, 36.7%) for the presence of activating mutations in exons 18, 19, 20 and 21 of the EGFR gene. Classic EGFR mutations (EGFRm) were detected in 11% (63/570) of the examined cases: 72% of the patients with an exon 19 deletion and 28% with an exon 21 L858R point mutation. Median age was 63 years. EGFR mutations were more common among young (<45 years old, 20.6%), female patients (23%) and non-smokers (37%). Furthermore, 96% of the patients with EGFRm tumors had adenocarcinoma and 4% had squamous cell carcinoma. All the patients with mixed histology or sarcomatoid differentiation were characterized as EGFR wild type. Overall, 41.3% of the EGFRm patients received EGFR-TKI as first-line treatment. Median PFS on first line EGFR-TKI was 9.6 months versus 3.1 months for patients receiving chemotherapy. However, there was no statistically significant difference in OS of EGFRm patients receiving EGFR TKIs as first or $\geq 2^{\text{nd}}$ line treatment (17.3 versus 18.6 months, $p=0.912$ , respectively). Median OS for EGFRm patients was 21.9 months (1.2-98.4 months) versus 13.5 months for patients with EGFRwt tumors (0.1-136 months; $p=0.031$ ).
<b>Conclusions:</b>	The prevalence of activating EGFR mutations in Greek patients with NSCLC is in accordance with previously published reports regarding non-Asians NSCLC patients. Treatment with EGFR-TKIs significantly improves the clinical outcome in the subset of NSCLC patients with EGFRm tumors.

# RENAL INSUFFICIENCY IN A PATIENT WITH RENAL CANCER TREATED WITH SUNITINIB AND THEN NIVOLUMAB, WITH SUSTAINED RESPONSE

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<b>Introduction:</b>	Sunitinib is one of the standard targeted therapies for metastatic renal cell carcinoma, whereas immunotherapy is a recently approved treatment.
<b>Aim:</b>	We report the case of a patient with metastatic renal cancer who presented with renal failure during sunitinib treatment and then nivolumab. However, he responded to these therapies.
<b>Methods:</b>	A 68-year-old man, with medical history of diabetes mellitus, hypertension and chronic renal insufficiency, was diagnosed with renal cell carcinoma with multiple lung metastases. He underwent left nephrectomy in November 2016 and he was addressed to the oncology department for further treatment. He started treatment with sunitinib 50 mg per day, 4 weeks/6, with initial creatinine clearance of 40 ml/min.
<b>Results:</b>	After 2 months of treatment creatinine level moved to 2.84 mg/dl and 2 months later to 3.43mg/dl. The patient developed proteinuria over 3 gr/24h. Sunitinib was discontinued and imaging reevaluation was performed, which revealed a complete response. Two months later, proteinuria reduced to 1.22 gr/24h. CT scan revealed progressive disease and she started second-line therapy with everolimus 5 mg/day. After 5 months of everolimus proteinuria increased again to 2.4 gr/24h. CT scan showed progression in the lungs and the patient became symptomatic (cough). He started 3d-line treatment with nivolumab 480 mg/28 days. After 3 cycles he developed acute renal failure with 11mg/dl of creatinine. Treatment was interrupted and the patient underwent hemodialysis. The new CT scans revealed partial response.
<b>Conclusions:</b>	Four cycles of targeted anti-angiogenic therapy with sunitinib led to complete response. Renal failure is not a frequent side effect of this drug. Safety of sunitinib continuation in patients with moderate to severe proteinuria has not been evaluated. This is also the case for immunotherapy, for which there is no data for creatinine clearance under 30 ml/min.

# REAL-WORLD DATA OF ERIBULIN TREATMENT IN PATIENTS WITH ADVANCED BREAST CANCER

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<b>Introduction:</b>	Eribulin is a new antineoplastic drug with a favorable toxicity profile and was approved by EMA in 2011 for HER2-negative advanced breast cancer after at least 2 prior lines of therapy (anthracyclines and taxanes). Later it was also approved in the second-line treatment, given that the above chemotherapeutic drugs were administered in either the early or metastatic setting.
<b>Aim:</b>	This study was undertaken in order to collect real-life data of safety and efficacy of eribulin treatment and compare them with clinical trials data.
<b>Methods:</b>	We performed a retrospective analysis of all patients who received eribulin in the 1 <sup>st</sup> Medical Oncology Department of Saint-Savvas Hospital between April 2014 and January 2019, for advanced histologically confirmed breast cancer. Each cycle consisted of the drug administration on days 1 and 8 and was repeated every 3 weeks. The study endpoints were progression-free survival (PFS), overall survival (OS), as well as toxicity profile. For survival analysis the Kaplan-Meier method was used.
<b>Results:</b>	In total 90 patients received the study treatment, of which 4 as 1 <sup>st</sup> -line, 18 as 2 <sup>nd</sup> -line, 33 as 3 <sup>d</sup> -line, 16 as 4 <sup>th</sup> -line, 8 as 5 <sup>th</sup> -line and 3 as 6 <sup>th</sup> -line treatment or beyond, whereas there was no data for the rest. The majority of patients had visceral metastases (liver, lungs). Median number of cycles is 6 (range 1-20). It should be noted that 5 patients received eribulin in combination with Trastuzumab for HER2-positive disease. Median PFS is 4 months (0-15) and median OS was not reached. Adverse events were as expected from the pivotal trials. No toxic death was observed.
<b>Conclusions:</b>	Eribulin is an effective treatment option in advanced breast cancer in the real patient population in our daily practice, including elderly patients and heavily pretreated patients.

# THE EFFECT OF CD44 PROTEIN AND OF PKM2 ENZYME ON THE PLATINUM-RESISTANT EPITHELIAL OVARIAN CANCER (EFC)

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**Introduction:** CD44, a surface marker for cancer stem cells interacts with PKM2, a key regulator of aerobic glycolysis and enhances the glycolytic phenotype of cancer cells that subsequently leads to increase of glutathione levels and decrease of ROS accumulation.

**Aim:** To explore the clinical importance of this interaction as a mechanism of drug resistance, we assessed the expression of PKM2 and CD44 in cancer cells of patients with epithelial ovarian cancer (EOC) treated with front line paclitaxel and carboplatin.

**Methods:** FFPE primary tumors from 172 patients with EOC were analyzed for PKM2 mRNA expression by qRT-PCR and evaluated for PKM2 and CD44 protein by immunohistochemistry.

**Results:** PKM2 mRNA and protein were detectable in the majority of patients while CD44 protein expression in 83% of patients. A significant positive correlation between PKM2 and CD44 protein expression (Spearman's test: -0.229;  $p=0.001$ ) was observed. High PKM2 mRNA and protein levels were significantly associated with lower progression free survival (PFS;  $p=0.001$  and  $p=0.008$ , respectively) and shorter overall survival (OS;  $p=0.005$  and  $p=0.001$ , respectively). Also, high CD44 protein expression was significantly correlated with shorter OS ( $p=0.004$ ) but not PFS ( $p=0.118$ ). Patients with high PKM2 and CD44 protein levels experienced shorter PFS and OS ( $p=0.005$  and  $p=0.001$ , respectively). Multivariate analysis revealed high mRNA expression of PKM2 as independent prognostic factor for decreased mPFS ( $p=0.041$ ) and mOS ( $p=0.038$ ).

**Conclusions:** PKM2 expression is a negative prognostic factor regarding the OS in EOC patients. These data further confirm that CD44 and PKM2 interaction may contribute to platinum resistance, a finding which have to be confirmed in future studies

# PALLIATIVE CARE IN OLDER PATIENTS WITH CANCER

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**Introduction:** Providing relief to the elderly with cancer is now imperative as the global population is getting older, and health professionals are being urged to cope with a multitude of patient problems based on palliative care principles.

**Aim:** To highlight the special issues of palliative care in elderly patients with cancer.

**Methods:** Bibliography was reviewed through the google scholar search engine and the «Pubmed» electronic database under the terms: Palliative care, aged, hospice, elderly, holistic, in English language for the years 2009-2018. 15 articles have been studied.

**Results:** The palliative care of the elderly with cancer demands a holistic and interdisciplinary approach as a fundamental principle and the improvement of quality of life is the ultimate goal. Integrated assessment and treatment of physical and mental symptoms is vital for the elderly. Aging adversely affects the symptoms of the disease and its multiple therapies. The elderly have co-morbidities and a multitude of complex symptoms that are often difficult to identify and treat. It is difficult to separate the problems associated with a newly diagnosed cancer in an elderly patient, from the normal problems caused by aging or other illnesses. Typical examples of difficult symptoms are dyspnea, nausea, vomiting and pain that can take various forms. At the same time, they often suffer from other chronic diseases such as cardiac, respiratory or renal failure. This makes them more vulnerable to disability and poor quality of life. Palliative care in the elderly with cancer should not be neglected and patients should have the right to «live until they die».

**Conclusions:** The physiology of aging affects the whole care of elderly cancer patients making palliative care a challenge. Increased awareness and effort by healthcare professionals is required for optimum results.

# USE OF PHARMACEUTICAL CANNABIS IN PALLIATIVE CARE

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<b>Introduction:</b>	Recently, there has been a growing beneficial use of cannabis in the management of symptoms in palliative care.
<b>Aim:</b>	To present the uses of cannabis in patients receiving palliative care.
<b>Methods:</b>	Bibliographic review was conducted through the «google scholar» search engine and the «Pubmed» electronic database under the terms: cannabis, cancer, palliative care, symptom management in English for the years 2011-2018. 18 articles were studied.
<b>Results:</b>	Cannabis use has been beneficial in palliative care. The literature mentions uses that lead to the improvement of patient's quality of life. This has led to increased cannabis use by these patients. The studies report the use of cannabis in advanced cancer patients with resistant symptoms in routine treatment and in hospice care. Such symptoms are dyspnea, nausea and vomiting, delirium and insomnia. It is used as tablets orally or sublingually, as a nasal spray and in inhaled form.
<b>Conclusions:</b>	Cannabis is increasingly used in palliative care with many benefits. However, patients, healthcare professionals and caregivers need to be aware of the benefits and consequences of using it to get the best results.

# ORAL MUCOSITIS–RELATED NEUROPATHIC PAIN IN HEAD AND NECK CANCER PATIENTS RECEIVING RADIOTHERAPY OR CHEMORADIOTHERAPY

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**Introduction:** Painful oral mucositis (OM) is a debilitating complication in Head and Neck Cancer (HNC) patients receiving RadioTherapy(RT)/ChemoRadioTherapy(CRT). Therapy-induced pain can be nociceptive and/or neuropathic. Neuropathic pain (NP) in HNC patients often remains underdiagnosed and undertreated.

**Aim:** To identify the OM-induced NP in HNC patients during RT/CRT.

**Methods:** Forty HNC patients during RT/CRT were included in the study. NP was evaluated using the Douleur Neuropathique 4 questionnaire (DN4q) as soon as patients reported moderate or severe pain on a 0-10 Numeric Rating Scale (NRS) 0-10, (NRS<sub>≥</sub>). Mucositis and xerostomia were assessed. Pain medication was recorded.

**Results:** Twenty-six patients (mean age 63.54 years) with moderate/severe pain answered a DN4q (mean NRS score 7.46). Five patients (19.23%) had a positive for NP, DN4q score  $\geq 4$ . The most common NP descriptor was “burning” (34.62%) followed by “electric shocks” (30.77%) and “pins-and-needles” (30.77%). Statistically significant ( $p < 0.05$ ) differences between positive and negative DN4q scores were observed for the “electric shocks”, “tingling”, “pins-and-needles” and “numbness” NP descriptors. Nine (34.62%) patients didn’t report any NP descriptors. A direct correlation was observed between DN4q score and intensity of pain, OM and xerostomia ( $p < 0.02$ ). Pain medication was administered to fifteen (15/26, 57.69%) patients. Adjuvant medication for NP was administered to 1 (1/5, 20%) patient with positive DN4q.

**Conclusion:** OM-induced NP was assessed for the first time during RT/CRT for HNC. Neuropathic pain was recorded in 5 patients with 1 of them receiving adjuvant NP medication. This study highlights the lack of adequate recognition and management of OM related NP.

# A MAN DIAGNOSED WITH LOCALLY ADVANCED GLOTTIC CANCER AND OGILVIE

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**Introduction:** Tumors of the oral cavity tongue are considered some of the most common head and neck tumors (3.9 / 100,000 people). The disease is usually diagnosed locally (31%) and the prognosis is poor. Where paraneoplastic syndrome occurs, this is either hypercalcaemia or a dermatological rash. Ogilvie is An acute dilation of the colon. A condition in which the patient is diagnosed with ileus without any evident mechanical cause of colorectal obstruction. The purpose of publishing this incident, is the scarcity of the syndrome in patients with head and neck cancer.

**Case:** A 39-year-old male and formerly alcoholic smoker came to the department due to locally advanced tongue cancer. The patient had already been subjected to a biopsy showing squamous cancer but also a thorough staging that did not show distant metastases . The patient reported difficulty swallowing and loss of fifteen kilograms in the last two months. The lesion was at the base of the tongue infiltrating epiglottis, nasopharynx and abnormal pituitary gland.

The patient when he first visited our clinic (02/2014) reported inability to discharge gases and faeces. From the clinical examination flatulence was observed, while the abdominal radiography showed that the patient had ileus. It could not be attributed to an electrolyte disorder nor to a mechanical obstruction, while computed tomography of the abdomen, magnetic resonance of the abdomen and colonoscopy showed no reason for the patient's ileum. Despite the patient's conservative treatment (fluid administration, intravenous claudication,levin) the ileum was not treated. The ileum was attributed to a paraneoplastic phenomenon -Ogilvie and so it was decided to start chemotherapy.

The patient started treatment with a 4-day cisplatin-5FU regimen on March 20, 2014, and from the first 24 hours his clinical condition improved. After the completion of five cycles of chemotherapy, the patient received concurrent chemotherapy-radiotherapy (08/2014, total dose of 60 Gy). Unfortunately, six months later, the patient relapsed locally. The man received two more chemotherapy regimens without any effect, and eventually died in 2016. Nevertheless, the patient had never been hospitalized for ileus and his disease was only recurring locally.

**Conclusions:** The three most common conditions associated with Ogilvie syndrome are non-operative trauma, infection and myocardial infarction. Severe pulmonary disease, malignancy and severe electrolyte imbalances have also been associated with Ogilvie syndrome but they are not that common. The case presented above is a rare case of a man with head and neck cancer that the symptoms resolved after chemotherapy.

# RHABDOMYOLYSIS, DERMATOMYOSITIS AND LOCALLY ADVANCED CANCER NASOPHARYNGEAL CANCER

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**Introduction:** Paraneoplastic syndromes are rare manifestations of symptoms which develop due to cancer. These symptoms may be endocrine disorders, gastrointestinal, haematological, musculoskeletal and dermatological disorders. It has been reported that 7.4% of patients with cancer will have a paraneoplastic symptom.

The most common paraneoplastic dermatological syndrome that occurs in patients with head and neck cancer is Bazex syndrome. It is psoriatic dermal keratosis of the limbs. The most common paraneoplastic haematological syndrome is hypercalcemia and leukocytosis. The effect is attributed to tumor production PHRP.

**Purpose:** The purpose of presenting this incident is the fact that the diagnosis of locally advanced cancer was made with concomitant manifestation of paraneoplastic syndromes.

**Case:** A 37-year-old male due to cervical bilateral lymphadenopathy was subjected to lymph node biopsy. The biopsy revealed squamous cell carcinoma (low differentiation) with immunohistochemical positivity in EBV LMP-1 protein, a finding that was compatible with non-keratinizing nasopharyngeal carcinoma. From the ENT examination no primary lesion was found. The patient was hospitalized due facial edema, disability to swallow and joint pain. From the clinical examination, peri-ocular edema and an extensive thoracic rash was found. From the laboratory test transaminasaimia was reported (SGOT: 472, SGPT: 105), elevation of LDH (958), while CPK was extremely elevated (CPK: 23,531). The patient did not report drop or use of toxic substances and despite the conservative treatment during his hospitalization there was no improvement. In addition, the patient underwent a skin biopsy that showed dermatomyositis. Finally, since there was no improvement of his blood exams and his condition seemed to deteriorate the symptoms were considered paraneoplastic and he started chemotherapy. As soon as the patient started chemotherapy with the regimen (carboplatin d1, 5-fu d1-4) the symptoms started to resolve.

It should be emphasized that despite his clinical improvement, his blood exams also had improved. The CPK enzyme after five days of chemotherapy was improved (CPK: 5201) and after 21 days, when he was hospitalized for the second cycle was almost normalized (CPK :402 and LDH: 332). At the same time the cervical lymphadenopathy and rash had also improved. The after having four cycles of chemotherapy he then had radiotherapy of the cervix given concomitantly with cisplatin (01 / 2017-03 / 2017).

Unfortunately, the patient's condition progressed in 05/2017 with liver and bone metastases. The man received another chemotherapy regimen (6 cycles of cisplatin-docetaxel - cetuximab) without any response and a few months later he died.

**Conclusions:** The purpose of presenting this incident is the unusual event of rhabdomyolysis and dermatomyositis as paraneoplastic syndrome and the immediate response to chemotherapy.

# ELDERLY CANCER PATIENTS GERIATRIC ASSESSMENT USING G8 SCREENING TEST: A PROSPECTIVE PILOT STUDY OF A.U.TH. MEDICAL ONCOLOGY CLINIC.

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**Introduction:** Elderly cancer patients are underrepresented in oncology clinical trials. Therefore, data regarding chemotherapy efficacy and toxicity is limited. G8-test is a screening tool used to identify elderly cancer patients who may benefit from a Comprehensive Geriatric Assessment.

**Aim:** The aim of this study was to investigate the prognostic value of G8 screening test in terms of one-year mortality and grade 3/4 toxicity.

**Methods:** Patients with solid tumors ≥ 70 years old, who received chemotherapy at the Department of Medical Oncology of the A.U.TH were enrolled to the study. The G8 screening test was applied prior to chemotherapy initiation. Patients with score ≤14 were considered frail. The primary end point of the study was overall survival (OS), defined as the time in months from chemotherapy initiation until death or last follow-up date.

**Results:** From November 2015 to April 2017, 40 patients were included in the study (median age 75, men 63%). Table shows patients' descriptive characteristics. Based on G8 score, 29 patients classified as frail and 11 as fit. Univariate analysis revealed shorter OS for frail patients (HR: 3.36 95%CI: 1.15-14.29, p=0.025) and greater hospitalization rates (54% *έναντι* 0%, chi-square p=0.006), compared to fit patients. On multivariate analysis, the G8 score maintained its independent prognostic value (HR: 4.38 95%CI: 1.24-27.69, p<0.049).

**Conclusions:** The G8 screening test is an independent prognostic marker associated with overall survival in patients with cancer ≥ 70 years old who are going to receive chemotherapy. This finding is particularly valuable taking into consideration the limited time and resources along with the absence of expertise for a Comprehensive Geriatric Assessment of elderly cancer patients in Greece.

	All N=40	Frail G8 ≤14 N=29	Fit G8>14 N=11
<b>Age</b>			
Mean ±SD	76 ± 4.3	73 ± 3	77 ± 4.3
<b>Gender</b>			
Men	25	17	8
Women	15	12	3
<b>ECOG PS</b>			
0-1	27	17	10
2-4	13	12	1
<b>Stage</b>			
Adjuvant	7	4	3
Metastatic	33	25	8
<b>Toxicity grade 3-4</b>			
No	18	11	7
Yes	21	18	3
<b>Hospitalization</b>			
No	26	15	11
Yes	14	14	0

# CORRELATION OF MEMORY T-CELL SUBPOPULATIONS WITH BREAST CANCER PATIENTS' RESPONSE TO THE AE37 VACCINE

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<b>Introduction:</b>	Vaccines constitute a promising therapeutic approach by triggering immune responses against cancer cells and their effect depends on patients' immune system state. The final goal of vaccines is the generation of a protective immune memory. Therefore the evaluation of T-cell subpopulations may be proved of great significance.
<b>Aim:</b>	Analysis of memory T-cell subpopulations in patients with breast cancer (BCa) before and during the inoculations against HER2 oncoprotein.
<b>Methods:</b>	The current study included BCa-patients, clinically disease-free, node-positive and high-risk node-negative with tumors expressing any degree of HER2. Patients were randomized and received either the AE37-modified peptide of HER2 with GM-CSF as adjuvant (n=39), or GM-CSF alone (n=36) in 6-monthly intradermal inoculations followed by 4 boosters administered every 6 months. Memory T-cell subsets (TNAIVE, TCM, TEM, TTEMRA & TSCM) were analyzed in peripheral blood via multicolor flow-cytometry, before vaccination, after the second inoculation, before the beginning of boosters and at the end of them. All of the subpopulations and their possible correlation with clinical outcome and other patients' clinicopathological characteristics were analyzed, aiming to predict the vaccine's effect.
<b>Results:</b>	The vaccine with AE37 affects selectively some of the subpopulations, while the adjuvant, even by itself, some others. Concerning boosters, the AE37 vaccine maintains the levels of TSCM, whereas it doesn't increase the percentage of TEMRA. The frequency of the subpopulations before the inoculations, as well as their change throughout vaccinations are related to the clinical outcome.
<b>Conclusions:</b>	The AE37 vaccine does not seem to negatively affect memory subpopulations, either by decreasing TSCM or by increasing TEMRA, while its clinical effect seems to be associated with the frequency of some subpopulations before and after the inoculations.

# GYNAECOMASTIA AS PARANEOPLASMATIC MANIFESTATION IN A PATIENT WITH NON-SMALL-CELL LUNG CANCER

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<b>Introduction:</b>	Gynaecomastia has been reported as paraneoplastic manifestation in gonadal and extragonadal carcinomas. Elevated levels of serum immunoreactive hCG, which is normally produced by the trophoblastic tissue of pregnant women, are detected in 12-14% of patients with non-small-cell lung cancer (NSCLC) due to ectopic production, while clinical manifestations of raised b-hCG, such as gynaecomastia, are uncommon.
<b>Aim:</b>	To present a case report of a patient with metastatic lung adenocarcinoma and gynaecomastia as paraneoplastic manifestation.
<b>Patients and methods:</b>	A 73-year-old smoker man, with a past medical history of chronic obstructive pulmonary and coronary artery disease, was diagnosed on July 2017 with stage IIIA (cT3N2M0) poorly differentiated lung adenocarcinoma, PDL-1 negative, without targetable driver mutations. As he was not eligible for the required pneumonectomy due to impaired lung function, he received neoadjuvant chemotherapy with the cisplatin/permetrexed/bevacizumab combination aiming to either downstage disease for less extended surgical treatment or to proceed to radical chemoradiotherapy. Unfortunately, after 2 cycles of chemotherapy the disease progressed with a solitary bone and an adrenal gland metastasis. Patient Subsequently received second-line treatment with nivolumab without response and consequently received salvage therapy with the docetaxel/hintedanib combination.
<b>Results:</b>	Patient complained for mastodynia and physical examination revealed bilateral gynaecomastia without any clinical signs of inflammation. <i>Hormonal tests</i> revealed an elevated serum b-hCG (17 MIU/ml), while a testicular ultrasound was normal. Analgesics were prescribed to alleviate breast pain. Patient succumbed due to NSCLC disease progression.
<b>Conclusions:</b>	Gynaecomastia is a rare paraneoplastic manifestation of NSCLC caused by ectopic b-hCG production. It may present either bilaterally or unilaterally, often on the tumor's side. Diagnostic assessment includes serum b-hCG and other gonadotrophins measurement and exclusion of other causes of gynaecomastia. It is treated symptomatically and it seems that it correlates to response to therapy.

# PRIMARY CARDIAC ANGIOSARCOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

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<b>Introduction:</b>	Primary heart angiosarcomas are rare cardiac neoplasms, known to carry an abysmal prognosis.
<b>Aim:</b>	We report the case of a young patient with metastatic cardiac angiosarcoma of the right atrium.
<b>Methods:</b>	A 33 year-old, never smoker male, with unremarkable past medical history, presented with gradually worsening dyspnea on exertion. The electrocardiography indicated negative T-waves, a transthoracic echocardiogram indicated the presence of a small pericardial effusion, while a CT scan revealed right pleural effusion, mediastinal lymphadenopathy and ascites.
<b>Results:</b>	Virologic testing, autoantibodies and immunologic studies were negative, while patient did not respond to treatment with ibuprofen, colchicine and empiric antibiotic therapy. A cardiac MRI depicted an infiltrating right atrial mass, while a PET scan indicated the presence of an 18FDG-avid lesion in the right lung and scapula. A subsequent endomyocardial biopsy performed with intravenous catheterization confirmed the diagnosis of primary heart angiosarcoma. Patient received weekly paclitaxel in combination with oral propranolol and a complete response was observed after 7 cycles of chemotherapy. Unfortunately, disease progressed after 8 months and second-line treatment with an epirubicin and ifosfamide combination was administered for an overall survival of 17 months.
<b>Conclusions:</b>	Heart angiosarcoma is a rare cardiac malignancy of endothelial origin, exhibiting a strong preference for middle-aged male patients and characterized by aggressive biologic behavior with high metastatic potential. Despite the variety of existing imaging studies, diagnosis remains challenging. Standardization of treatment strategy in prospective studies is warranted, with the ultimate goal of improving survival outcomes and quality of life.

# CONCURRENT COLORECTAL AND RENAL CELL CARCINOMA BOTH RESPONDING TO TREATMENT WITH PAZOPANIB AND AXITINIB

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<b>Introduction:</b>	Numerous tyrosine kinase inhibitors (TKIs) are used for the treatment of metastatic renal cell carcinoma (RCC) while regorafenib is licensed for the treatment of previously treated metastatic colorectal cancer (CRC). The activity of pazopanib and axitinib in advanced CRC has been studied in phase I-II studies.
<b>Aim:</b>	To present an interesting case of a patient with concurrent kidney and colon cancer both responding to treatment with TKIs.
<b>Patients and methods:</b>	A 69 years old smoker male underwent a left nephrectomy in June 2017 due to the presence of a renal mass. The histopathological examination confirmed the presence of a grade 3, pT3Nx, clear-cell carcinoma, while CT scans revealed bilateral pulmonary metastases and a hepatic flexure colon mass. A colonoscopy identified a mass in the transverse colon covering three quarters of the lumen and the histological report confirmed the presence of a moderately differentiated invasive colon adenocarcinoma.
<b>Results:</b>	A CT-guided lung lesion biopsy was consistent with RCC metastatic disease. In view of the asymptomatic colon cancer and the rapidly imaging deterioration of the metastatic renal cancer, treatment with pazopanib commenced with acceptable toxicity and partial response of both the renal metastatic disease and the colonic primary tumor. Eight months later, imaging tests revealed progression of the metastatic disease while the colon mass was further responded. Patient received second-line treatment with Axitinib with new partial response of the metastatic disease while a colonoscopy revealed a complete remission of the colon cancer. Patient continues treatment with Axitinib with good tolerance and lasting response.
<b>Conclusion:</b>	Treatment with pazopanib and with axitinib in this patient achieved significant response in metastatic RCC and local colon cancer, confirming the activity of TKIs in both diseases.

# MALIGNANT TRANSFORMATION OF SCHNEIDERIAN PAPILLOMA

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<b>Introduction:</b>	Schneiderian papillomas (SPs), arising from the ectodermally derived respiratory mucosa, account for 0.4-4.7% of all sinonasal tract tumors. The vast majority of patients are males, smokers and aged 50-60 years old. Synchronous or metachronous malignant transformation of SPs, usually to squamous cell carcinoma (SCC), is identified in less than 10% of reported cases. The precise nature of this oncogenic transformation has not been clearly defined, thus there is an unmet need for further studies into pathogenetic factors of SP-derived SCCs, including the ambiguous role of human papilloma virus infection. In daily clinical practice, treatment approach depends on tumors' site, extent of disease and surgical experience. Nevertheless, prognosis of SP-derived SCCs remains poor.
<b>Aim:</b>	We present the case of a patient with a SP-derived SCC.
<b>Methods:</b>	A 61-year-old male, smoker, with a history of post-traumatic mydriasis of right eye, presented with progressive binocular diplopia, blepharoptosis and amblyopia over the past 4 months. He had recently underwent intranasal papilloma-plucking (polypectomy) and the histopathological examination of the resected «nasal polyp» confirmed the presence of squamous cell carcinoma arising from a Schneiderian papilloma.
<b>Results:</b>	CT scan and MRI revealed an 11 cm tumor extending from the ethmoidal air cells to the ground of the oropharynx, eroding the maxillary, frontal, ethmoid and sphenoid- bones and the clivus, and resulting in nasal airway obstruction. The patient received concurrent chemoradiotherapy with cisplatin/5-fluorouracil with good tolerance and he achieved a partial disease remission.
<b>Conclusions:</b>	A patient with locally-advanced SP-derived SCC, presenting with progressive binocular diplopia and blepharoptosis, was treated with concurrent chemo-radiotherapy with satisfactory results.

# ERECTILE DYSFUNCTION IN PATIENTS WITH PROSTATE CANCER UNDERGOING PELVIC RADIOTHERAPY. SEARCH FOR TREATMENT OPTIONS

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<b>Introduction:</b>	Prostate cancer is the second most common type of cancer in the male population. Radiation therapy, however, causes a) injury to endothelial cells and smooth muscle fibers, b) rupture of smaller vessels in the area of the prostate and penis, c) subsequent vascular stenosis and arterial insufficiency, d) reduction of the cavernous nerve kinetic response, e) damage to peripheral nerve fibers, eventually leading to erectile dysfunction.
<b>Aim:</b>	To search for and summarize the therapeutic options for radiation-induced erectile dysfunction in prostate cancer patients, with a view to improving their quality of life.
<b>Methods:</b>	This paper uses material from the Pubmed / MEDLINE database. The paper is a bibliographic review by 12/2018. A careful selection was made of the data used, based on their validity, their scientific documentation and the correct statistical analysis of the data.
<b>Results:</b>	The strategy for management of radiation-induced erectile dysfunction is organized on many levels. These include: conservative management with physical exercise and psychosocial treatment and counseling, oral use of pharmaceutical formulations of PDE-5i inhibitors, use of a vacuum pump device or pump, intraurethral suppositories, intracavernosal infusion, as well as a combination of all the above. Experimental data highlights potential future treatment options after injecting stem cells derived from adipose tissue, as well as the use of nanotechnology as a "carrier" of pharmaceuticals in target cells.
<b>Conclusions:</b>	Erectile dysfunction is a frequent side effect in the prostate cancer patient who has undergone radiation therapy. In modern times, the elucidation of the mechanisms of erectile dysfunction due to radiation has contributed to the improvement of newer techniques and the development of new therapeutic options, offering the doctor a therapeutic armamentarium on the one hand, and the patient the choice of treatment on the other hand.

# SLEEP DISTURBANCES AND CANCER

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<b>Introduction:</b>	Sleep disturbances represent an important problem in cancer patients. The aim of this review was to evaluate the main changes in the sleep cycle of the oncologic patients.
<b>Materials and methods:</b>	We reviewed into the current literature in pubmed/MEDLINE until 12/2018. Our review was solely based on published articles in the English language. The research included all cancer types. The majority of the articles referred to breast and prostate cancer.
<b>Results:</b>	Mixed effects were observed concerning the quality of the sleep of the patients. These problems are referred below: a) increase of the initiating time, b) time it takes to fall asleep, c) awakening during sleep time, d) agitated and inadequate sleep and e) daytime somnolence. Fatigue and pain were the two main etiologic factors in all the patients. Apart from that, coexistence of chronic diseases like arterial hypertension, diabetes mellitus, coronary artery disease, depression as well as loss of concentration was deteriorating the cycle and the quality of the sleep. Patients having undergone surgery presented more serious complications in their sleep cycle.
<b>Conclusions:</b>	Oncologic patients have a poor overall sleep quality with more prevalent dysfunctions being daytime somnolence and difficulties in maintaining sleep. This is the reason why there is a need for routine screening of the cognitive behaviour and for any sleep disturbance of the patients in order to improve their sleep quality.

# DETECTION DLL3+ CIRCULATING TUMOR CELLS AND EVALUATION OF THEIR CLINICAL VALUE IN SMALL CELL LUNG CANCER PATIENTS UNDER FRONT LINE TREATMENT

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<b>Introduction:</b>	DLL3 is a surface protein of various cancer cells, including small cell lung cancer (SCLC). DLL3 is not expressed by normal cells, and thus is considered as a potential marker for the treatment evaluation in SCLC patients.
<b>Aim:</b>	To characterize and evaluate the presence of DLL3-positive Circulating Tumor Cells (CTCs) and tissue biopsies in SCLC patients receiving front-line chemotherapy and assess their clinical relevance.
<b>Methods:</b>	Peripheral blood was obtained from 108 treatment-naïve patients with SCLC, after one-etoposide/platinum cycle and on disease progression. CTCs were detected following immunofluorescence staining using antibodies against the DLL3, cytokeratins (CK), CD45 and vimentin (Vim). DLL3 expression was also evaluated in tissue biopsies of 20 SCLC patients using immunohistochemistry.
<b>Results:</b>	Before treatment, 74.1% and 70.0% of patients had DLL3+/CD45- CTCs and DLL3-high tissue expression, respectively. Among DLL3-high patients, 85.7% had DLL3+/CD45- CTCs. One-treatment cycle significantly decreased both the detection rate of DLL3+/CD45- CTCs ( $p < 0.001$ ) and their absolute number ( $p < 0.001$ ). Triple immunofluorescence staining revealed an important CTC heterogeneity since DLL3 could be detected in Vim+, Vim-, CK+ and CK- CTCs. On disease progression, both the detection rate of DLL3+/CD45- CTCs as well as their number were significantly increased compared to post-1st cycle values ( $p < 0.001$ and $p = 0.002$ , respectively). Multivariate analysis revealed the detection of DLL3+/CD45- CTCs at baseline was an independent factor for decreased progression-free survival (HR= 10.8; $p = 0.005$ ) whereas their detection on disease progression was an independent factor for decreased overall survival (HR: 28.2; $p = 0.016$ ).
<b>Conclusions:</b>	The results of the current study demonstrate an important heterogeneity of CTCs, based on the expression of CK, Vim and DLL3, in patients with SCLC. Moreover, the changes of DLL3+/CD45- CTCs during treatment seem to be a dynamic biomarker associated with treatment efficacy and patients' clinical outcome.

# CURECANCER: AN ONLINE TOOL WITH A SUPPORTIVE CARE MISSION

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<b>Introduction:</b>	While working in a dental oncology office we realized the need for practitioners to know their patients' medical history and the difficulty to obtain this information. Patients during active or after cancer therapy or long-term survivors struggled with collating details related to the complex cancer and supportive care treatments and other key information. CureCancer, a patient-centered tool, was inspired.
<b>Aim:</b>	We aimed to help patients self-create their medical profile and treatment plan and communicate their profile to health care professionals (HCPs) within or outside the oncology setting.
<b>Methods:</b>	Information to be recorded was identified and included patient demographics, cancer type and stage, co-morbidities, cancer therapies and medications, phase of therapy, symptoms and laboratory examinations. The Agency of Personal Data protection was contacted to ensure data protection and secure keeping.
<b>Results:</b>	The CureCancer tool, <a href="http://www.curecancer.gr">www.curecancer.gr</a> , <a href="http://www.curecancer.eu">www.curecancer.eu</a> , was created and can function from a desktop or a mobile application. Patients can record and update their medical information and status, upload laboratory examinations, track their symptoms and share files to facilitate the HCPs. Patient to patient communication, patient-focused information on toxicities, and news on the continuous progress of cancer therapies were included in the platform.
<b>Conclusion:</b>	A new online, patient-driven tool helps patients file their treatment plan and communicate their medical records with the HCPs. CureCancer can enhance the success of anticancer therapy, minimize toxicities and reduce HCPs' burden. A study was initiated, in collaboration with cancer hospitals and patient associations, to assess feasibility, patient and physician satisfaction, and usefulness of the tool.

# NGS BASED TUMOR MOLECULAR PROFILING IN PATIENTS WITH NSCLC USING LIQUID BIOPSIES

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<b>Introduction:</b>	Analysis of circulating tumor DNA/RNA in plasma of cancer patients is the most widespread and documented form of "liquid biopsy" and provides real-time information on the molecular profile of the tumor.
<b>Aim:</b>	The aim of this study was to determine the sensitivity and specificity of the liquid biopsy for the detection of tumor mutations. In addition, the clinical utility of analyzing multigene panels using Next Generation Sequencing technology (NGS) was investigated in patients with NSCLC with acquired resistance to targeted therapy.
<b>Methods:</b>	Analysis of 12 genes and 3 translocations ( <i>ALK</i> , <i>ROS1</i> , <i>RET</i> ), was performed using NGS in plasma and tumor tissue of 35 patients with Non-Small Cell Lung Cancer (NSCLC) before treatment. Additionally, NGS analysis was carried out in 20 patients with NSCLC who harbored an EGFR mutation at diagnosis and had received TKI targeted treatment but did not present the p.T790M resistant mutation after treatment using the CE-IVD COBAS EGFR Mutation Test v2.
<b>Results:</b>	Among the 35 NSCLC patients who had not received targeted treatment, the concordance between the molecular profile obtained in tumor and plasma was obtained in 82% of the cases. Furthermore, among patients with an EGFR mutation at diagnosis, who have received TKIs treatment but had not detectable levels of the T790M mutation by the COBAS method, the use of NGS allowed the detection of this mutations in 2 patients. Therefore these patients could benefit from third-generation TKIs. Applying this gene panel allowed the elucidation of the resistance mechanism in 6 of these patients who carried mutations in other genes, possibly associated with resistance to treatment, such as <i>BRAF</i> , <i>PIK3CA</i> , <i>MAPK1</i> and <i>TP53</i> .
<b>Conclusions:</b>	NGS techniques can be used to reliably detect tumor mutations in liquid biopsy thus providing clinically relevant information both before and after use of therapy in patients with NSCLC.

# MULTIGENE TESTING FOR HEREDITARY BREAST CANCER: MORE GENES MORE INFORMATION IN 871 CASES

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<b>Introduction:</b>	Nowadays, the application of Next Generation Sequencing (NGS) technology has facilitated multigene panel analysis and is widely used in clinical practice for the identification of individuals with an inherited predisposition to cancer.
<b>Aim:</b>	The aim of this study was to highlight the usefulness of multigene analysis and to investigate the extent and nature of mutations in individuals with a personal and/or family history of breast cancer.
<b>Method:</b>	Analysis of 33 genes involved in hereditary cancer predisposition was performed using NGS. A capture based NGS technology was used for the analysis of 33 genes involved in hereditary cancer predisposition, in 768 individuals with personal history of breast cancer and in 103 individuals with family history of the disease.
<b>Results:</b>	<p>A high prevalence of <i>BRCA1/2</i> pathogenic variants was observed in both patients with personal and family history of breast cancer (12.6% and 8.7% respectively). In total, at least one pathogenic variant was detected in 24.7% of breast cancer affected individuals and 14.6% of those with family history of breast cancer. In 48.3% of the individuals with a pathogenic variant, the finding was detected in genes other than <i>BRCA1/2</i>. In addition to <i>BRCA1/2</i> other frequently mutated genes were <i>PALB2</i>, <i>CHEK2</i>, <i>MUTYH</i> and <i>ATM</i>. In 8.3% of the positive patients, two pathogenic mutations were identified which explained not only the personal history of cancer but also the family history showing diverse cancer types.</p> <p>Of notice is also the relatively high percentage of large genomic rearrangements (LGR) identified, since 6.3% of the individuals with a positive finding carried this type of alteration. This indicates that the analysis of LGR is essential in any comprehensive genetic testing approach.</p>
<b>Conclusions:</b>	90% of the positive findings in Breast Cancer patients detected in this study were in genes included in the NCCN Clinical Practice Guidelines for Breast and Ovarian Cancer enabling patients' clinical management based on their genetic background. The detection of inherited mutations using NGS technology gives clinically relevant information to the individual tested and the relatives at risk, concerning management and treatment approaches.

# STUDY OF EFFICACY AND SAFETY OF AXITINIB BEYOND THE SECOND LINE IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA

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**Introduction:** Axitinib is a selective inhibitor of VEGF1,-2 and -3 receptors, which is approved as a second line therapy for patients with metastatic Renal cell carcinoma (mRCC).

**Aim:** Study of the efficacy and safety of Axitinib as 3<sup>rd</sup> line therapy and beyond

**Methods:** This is a retrospective study of patients with mRCC who received Axitinib to our department as 3<sup>rd</sup> line or beyond from December of 2013- January of 2017. Patients' medical files were used to record demographic, clinicopathological characteristics and survival data. Log-rank test was used to count survival differences.

**Results:** A total of 22 patients enrolled in the study with median age 55.4 years. All patients were subjected to nephrectomy, 17 (85%) had renal cell carcinoma en superiority. At the start of the first line therapy, based on the criteria IMDC, 6 patients were in favorable prognostic group, 13 in the intermediate and one poor. 12 patients (55%) received Axitinib as third line treatment and the rest in subsequent lines. Half of the patients had received at least two therapy lines with VEGF-TKIs before the administration of Axitinib. Based on the RECIST criteria, 6 patients (27%) showed partial response to Axitinib treatment and 9 patients (41%), stable disease. 4 patients had ongoing responses for over a year. Median survival time without disease progression (mPFS) was 6.3 months (95% CI 3,6-8,9) and the median overall survival (mOS) after initiation of Axitinib was 21.5 months (95% CI 11, 9 to 31.3). The response to treatment and the duration of survival was independent of the treatment line to which Axitinib was administered or the number of previous TKIs. The most common toxicities regardless of the grade were fatigue (11 patients, 50%), hypertension (five patients, 23%), hypothyroidism (5 patients, 23%), palmar-plantar erythrodysesthesia syndrome (4 patients, 18%) and hoarseness (18%).

**Conclusions:** On the basis of daily clinical practice data, Axitinib is an effective and safe treatment option for patients with mRCC even after the second line, providing long lasting responses in a category of patients.

# EVALUATING WOMEN'S BELIEFS AND ATTITUDES IN THE PREFECTURE OF SERRES TOWARDS BREAST CANCER SCREENING USING THE HEALTH BELIEF MODEL

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<b>Introduction:</b>	Breast cancer is the most common form of neoplasm in women and the most frequently diagnosed cause of death worldwide. Screening is considered necessary in order to reduce the mortality.
<b>Aim:</b>	The purpose of the research is to study women's attitudes and beliefs towards the effectiveness of screening, their awareness of breast self-examination and mammography, and the factors of their satisfaction (or dissatisfaction) from the mammography department.
<b>Methods:</b>	A questionnaire survey was conducted on 110 female patients who had their mammography at the General Hospital of Serres and the Health Centers in the Prefecture of Serres.
<b>Results:</b>	The results have shown that the majority of women, especially those of high educational level, consider mammography and breast self-examination as highly important for the early diagnosis of the disease. However, the feeling of vulnerability is not particularly high, as most women do not feel vulnerable to the disease due to a lack of information. Furthermore, the perception of the severity of the disease is moderate and demonstrates a high positive pertinence to age. Lastly, the experience and training of the radiologists in the Department of Mammography was considered the most important factor of satisfaction.
<b>Conclusions:</b>	The originality and contribution of this study lies in the fact that the awareness of women's attitudes and beliefs regarding prevention is limited, as the issue is little researched in Greece, especially in the borderlands where accessibility to health structures is limited. Its usefulness pertains to the potential use of its results for designing and carrying out interventions to inform the general population in order to reinforce prevention and reduce the incidence of the disease.

# NEUROENDOCRINE CARCINOMAS OF THE GYNECOLOGIC TRACT: A SINGLE CENTRE EXPERIENCE

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**Introduction:** Neuroendocrine carcinomas of the gynecologic tract are a rare (2%), heterogeneous group of neoplasms. Limited data exist in the literature to guide therapeutic decisions.

**Aim:** We performed a retrospective analysis of poorly differentiated neuroendocrine carcinomas that were treated in our department.

**Methods:** Medical records of women with neuroendocrine carcinomas treated at Alexandra Hospital from 1995 to 2016, were retrospectively identified. Clinicopathological data, treatment and survival data were analyzed.

**Results:** In the analysis, 16 patients were included. Ten patients were diagnosed with neuroendocrine carcinomas of cervical origin, three of endometrial and three of ovarian. Five patients (31.3%) had stage I disease (4 cervical, 1 ovarian), four (18.8%) stage II (1 endometrial, 2 cervical, 1 ovarian), four (25.1%) stage III (2 endometrial, 2 cervical) and three (18.8%) stage IV (2 cervical, 1 ovarian). Patients with ovarian neuroendocrine carcinomas were treated with surgery followed by adjuvant paclitaxel-carboplatin chemotherapy (apart from the stage I patient). From the 13 patients with uterine or cervical neuroendocrine carcinomas, 2 patients had de novo metastatic disease and one received chemotherapy. The 11 remaining patients with local disease were treated with either surgery followed by etoposide-platinum chemotherapy with or without radiotherapy (6 patients) or surgery and radiotherapy (2 patients) or radical radiotherapy (3 patients). Median Disease-Free Survival (mDFS) in the whole population of uterine and cervical neuroendocrine carcinomas was 12 months and median Overall Survival (mOS) 14.9 months.

**Conclusions:** Neuroendocrine carcinomas of the gynecologic tract have aggressive behavior, with 50% of the patients to be diagnosed at stage III or IV. Responses in systematic therapy are poor and more effective therapies should be sought.

# NON-SMALL CELL LUNG CANCER IN ELDERLY PATIENTS $\geq 75$ YEARS OLD: DISEASE CHARACTERISTICS AND TREATMENT RESULTS FROM ARIADNE DATABASE

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<b>Introduction:</b>	Non-small cell lung cancer (NSCLC) is a common disease in the elderly.
<b>Aim:</b>	To present population-based data on disease characteristics and treatment results in elderly NSCLC patients.
<b>Methods:</b>	We retrospectively analyzed data from the ARIADNE database that included NSCLC patients treated in 4 oncology centers in Crete, between 2005-2014.
<b>Results:</b>	Three hundred and seven out of 1555 NSCLC patients (20%) were $\geq 75$ (range 75-90) years old. Among them, males were 89% and active or ex-smokers were 80%, while 57% and 39% had adenocarcinoma and squamous cell carcinoma, respectively. Disease stage was I-II, IIIA, IIIB and IV in 18%, 13.4%, 10.5% and 58.2%, respectively. Ten out of 102 (9.8%) tumor specimens examined harbored activating EGFR mutations while no ALK rearrangements were detected in 36 examined samples compared to 11.2% and 4.3%, respectively, in patients $< 75$ years old. Fifty six out of 97 (58%) patients with stage I-III disease underwent surgical treatment and among them 16 (28.5%) consequently received adjuvant chemotherapy. Twenty-six out of 73 (35.6%) patients with stage IIIA/IIIB disease were treated with concurrent chemoradiotherapy, while 12 (16.4%) received only radiotherapy. One hundred and eighty-five patients received 1st-line chemotherapy (which in 48.6% of cases consisted of cisplatin-based combinations), while 24.3% and 10% of them consequently received 2nd-line and 3d-line treatment, respectively. Thirty-nine (12.7%) patients received treatment with TKIs during the course of the disease. Median survival of patients $\geq 75$ years old, for all disease stages, was 11 months (12/8.3/6.8 months for 75-80/81-85/ $> 85$ years old age-groups, respectively; $p=0.063$ ).
<b>Conclusions:</b>	NSCLC patients $\geq 75$ years old in Crete presented similar disease characteristics with historical data from developed countries while they received less intensive treatment compared to what is considered as standard of care treatment per disease stage. Advanced age was non-significantly correlated with inferior survival.

# FIRST-LINE TREATMENT WITH MODIFIED FOLFIRI PLUS BEVACIZUMAB OR PANITUMUMAB IN PATIENTS ≥70 YEARS OLD WITH METASTATIC COLORECTAL CANCER: RESULTS OF TWO PARALLEL PHASE II TRIALS FROM HELLENIC ONCOLOGY RESEARCH GROUP

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**Introduction:** Data on combination chemotherapy plus biologics for the treatment of elderly patients with metastatic colorectal cancer (mCRC) are limited.

**Aim:** We present the efficacy and safety results of two parallel phase II trials of modified (m)FOLFIRI plus bevacizumab or panitumumab as 1<sup>st</sup>-line treatment in elderly patients with mCRC.

**Methods:** Patients ≥70 years old with unresectable mCRC were treated with bevacizumab (5mg/Kgr) in tumors with KRAS/RAS mutant or unknown status (study A) or Panitumumab 6mg/kg as 60min iv infusion in KRAS/NRAS wild type tumors (study B) followed by mFOLFIRI (Irinotecan 130mg/m<sup>2</sup> as 90min iv infusion, Leucovorin 400mg/m<sup>2</sup> as 2h iv infusion and 5-Fluorouracil 400mg/m<sup>2</sup> as bolus iv infusion on day 1 and 5-Fluorouracil 1.200 mg/m<sup>2</sup> as continuous iv infusion for 46h), every 2 weeks. The primary endpoint was overall response rate (ORR). Sample size calculation was based on the mini-max Simon two-step design: The null hypothesis was that the ORR is ≤30% versus the alternative hypothesis of ORR ≥50% ( $\alpha = 0.05$ , power 80%).

**Results:** Patients characteristics, efficacy and toxicity results as per table.

**Conclusions:** The mFOLFIRI plus bevacizumab or panitumumab combination presented significant efficacy with manageable toxicity as 1<sup>st</sup>-line treatment in patients ≥70 years old with mCRC.

	mFOLFIRI plus Bevacizumab (n=42)	mFOLFIRI plus Panitumumab (n=44)
Analyzed	n=31	n=44
<b>Patients Characteristics (%)</b>		
Mean age (range), years	75 (70-84)	76 (70-88)
ECOG PS 0/1/2	39/58/3	25/71/4
Male/Female	81/19	73/27
Rectal Cancer	16	25
Primary tumor not resected	26	16
<b>Efficacy</b>		
Overall Response Rate (95% CI), %	41.9 (24.6%-59.3%)	47.7 (32.9%-62.5%)
Stable Disease, %	38,7	15.9
PFS (95% CI), months	8.6 (7.6-9.6)	6.1 (3.6-8.7)
OS (95% CI), months	28.8 (16.5-41.1)	20.9 (11.7-30.1)
1-year survival, %	77.4	68.2
Median Follow up, months	39.5	36.0
<b>Grade 3-4 Adverse Events (%)</b>		
Neutropenia	19.3	9.0
Diarrhoea	-	20.4
Mucositis	-	2.3
Skin toxicity	-	4.5
Fatigue	-	4.5
Bowel perforation	-	2.3
Paronychia	-	2.3
Constipation	3.2	-
Hypertension	3.2	-

# DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF HUR PROTEIN EXPRESSION IN SALIVARY GLAND TUMOURS

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<b>Introduction:</b>	HuR protein is involved in the post-transcriptional regulation of several genes expression, altering the expression of oncogenes, growth factors, apoptotic and angiogenic factors. Consequently, HuR expression is correlated with carcinogenesis, prognosis and resistance to chemotherapy in cancer patients. Research data on the role of HuR protein in salivary gland tumours (SGTs) remain limited, whereas there is a paucity of information regarding its prognostic significance.
<b>Aim:</b>	To investigate the potential diagnostic and prognostic significance of HuR protein immunohistochemical expression in SGTs.
<b>Methods:</b>	HuR protein expression was assessed immunohistochemically in 50 histological SGT samples [(29 benign (16 sialadenomas papilliferum, 5 Warthin tumours, 1 basal cell adenoma, and 7 oncocytomas) and 21 malignant (2 basal cell adenocarcinomas, 6 mucoepidermoid carcinomas, 7 squamous cell carcinomas, 3 acidic carcinomas and 3 adenoid cystic carcinomas)] and was statistically correlated with the patients' clinicopathological characteristics for all cases and survival for malignant SGTs.
<b>Results:</b>	Nuclear pattern of HuR immunostaining was observed in all (50/50, 100%) and cytoplasmic in 42.5% (20/47) of SGTs. Cytoplasmic pattern of HuR immunostaining was more often found in malignant (63.16%, 12/19) compared to the benign (29.63%, 8/27) SGTs ( $p=0.024$ ). Accordingly, the cytoplasmic HuR H-score was higher in malignant when compared with benign SGTs ( $p=0.031$ ). Significant difference was also found in cytoplasmic HuR H-score between low grade (LG) and high grade (HG) SGTs ( $p=0.003$ ). Similar observations were also noted for nuclear HuR H-score, which was higher in malignant ( $p=0.006$ ) and especially in HG ( $p=0.008$ ) SGTs. Finally, in survival analysis cytoplasmic HuR H-score was correlated with unfavourable patients' with malignant SGTs prognosis ( $p=0.022$ ).
<b>Conclusions:</b>	HuR protein seems to have a diagnostic role discriminating malignant and benign SGTs and additionally, is correlated with a more aggressive phenotype, emerging as a significant factor of adverse prognosis for patients with malignant SGT.

# ENDOMETRIAL CANCER WITH HIGH MICROSATELLITE INSTABILITY (MSI-H): SIGNIFICANT RESPONSE TO PEMBROLIZUMAB TREATMENT

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<b>Introduction:</b>	Endometrial cancer is the most common gynecologic cancer in developed countries. A percentage of up to 30% show high microsatellite instability (MSI-H). In clinical trials of PD-1 inhibitor pembrolizumab, including patients with advanced solid MSI-H tumors, patients with endometrial cancer demonstrated a response rate of 36%.
<b>Aim:</b>	Presentation of patient with advanced endometrial cancer and therapeutic approach based on the novel indication of Pembrolizumab in MSI-H tumors.
<b>Results:</b>	A 72 year old female patient was diagnosed in 2011 with endometrial cancer. She underwent total hysterectomy and bilateral salpingo-oophorectomy and the histological examination revealed endometrioid adenocarcinoma. In 2012, there was local recurrence in the vagina. External radiotherapy and brachytherapy were given. In 2015, the disease relapsed with lung metastases. The patient received 6 cycles of Cisplatin/Adriamycin, with partial response in lung lesions. Then there was a progression of the pulmonary disease, with the patient receiving second line treatment with weekly Paclitaxel. Hormone therapy was also tested. In 2018, there was severe deterioration, with newly emerging liver lesions. Third-line chemotherapy with Topotecan was given, but further imaging and clinical deterioration was recorded, with intense fatigue and abdominal pain. Molecular control was performed, using the tissue specimen from the initial histological examination, and identified MSI-H. The patient received 4 cycles of Pembrolizumab with good tolerance, from July to September 2018. In October 2018, there was significant response in both lung metastases (the largest lesion 3.6 vs 6 cm) and liver metastases (the largest lesion 1.6 vs 4.6 cm), impressive decrease in the value of tumor markers (CA125 11 versus 423 and CA15-3 73 versus 872), and impressive clinical improvement. The patient continues her treatment to date.
<b>Conclusions:</b>	Patients with advanced endometrial cancer, particularly endometrioid type, should be screened for MSI. MSI-H patients have a significant chance of benefit from Pembrolizumab treatment.

# A RARE CASE OF A PATIENT WITH SYNCHRONOUS DIAGNOSIS OF BREAST AND RENAL CANCER

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**Introduction:** Synchronous appearance of multiple cancers in a patient is a rare phenomenon. Synchronous tumors are defined as the presence of a second tumor at the same time as the first, or within the first 6 months after the first tumor diagnosis. The incidence of multiple primary malignant tumors increases with age. Presence of family history and genetic predisposition are factors associated with increased risk of occurrence. Breast cancer is the most common malignancy in women, whereas renal clear cell carcinoma is the most common renal tumor. Synchronous presence of breast cancer together with one or more types of cancers such as colon, lung, liver, has been described in the literature. Presence of kidney cancer with synchronous or metachronous cancers in the above organs has also been reported in the literature. However, reports of synchronous breast and kidney cancer are very rare.

**Aim:** Presentation of a rare case of a patient with synchronous breast and kidney cancer and their treatment.

**Results:** A 68 year old female patient was diagnosed a year ago with breast cancer. The patient underwent lumpectomy and sentinel lymph node biopsy. Histological examination revealed breast carcinoma pT1bN0, ER (+), PR (+), HER-2 positive. Computer tomography imaging highlighted extensive neoplastic tumor in the right kidney. The patient underwent right nephrectomy, with the histological examination revealing clear cell renal carcinoma pT2a. The patient received adjuvant chemotherapy for breast cancer with Docetaxel-Carboplatin-Herceptin and then she received radiotherapy. Subsequently, the patient continued and completed Herceptin treatment, and started hormone therapy, which continues to date. The last computer tomography follow up examination, one month ago, was negative for relapse. Tumor markers were within the normal range (CEA: 1.8 ng / ml, CA 125: 7.9 U / ml, CA 15-3: 18, 7 U / ml).

**Conclusion:** The presence of synchronous breast and renal cancer is very rare. Early diagnosis and treatment, according to the guidelines, have good results in these patients.

# CUSTOMISATION OF THERAPEUTIC STRATEGY IN METASTATIC COLORECTAL CANCER BY USE OF LIQUID BIOPSIES (DETECTION OF RAS MUTATIONS WITH DIGITAL PCR AND NGS)

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<b>Introduction:</b>	Metastatic colorectal cancer (mCRC) ranks among the most frequent and lethal neoplasms worldwide, with development of metastatic disease in 50% of cases. Monoclonal antibodies against the epidermal growth factor receptor (EGFR) cetuximab and panitumumab can offer significant benefit to <i>RAS</i> wild-type tumours. However, given the cancer heterogeneity and clonal evolution, molecular characterisation of archival tumour tissue is deemed insufficient to guide treatment decisions in the course of the disease. The study of tumour biological material from blood, also known as liquid biopsy, can alter the facies of oncology in the years to come.
<b>Aim:</b>	Plasma samples from 40 patients with mCRC were tested for <i>KRAS</i> and <i>NRAS</i> mutations at diagnosis with matched tissue, mid first-line of treatment, and at disease progression. Additional next-generation sequencing panel testing was performed in a subgroup of patients, in tissue and plasma, at baseline and disease progression. This information was analysed in association with clinicopathological data, response and survival parameters, to explore how liquid biopsies could be used to optimise targeted therapeutic management in this disease setting.
<b>Methods:</b>	Baseline tissue testing was based on real-time polymerase chain reaction (PCR) or nextgeneration sequencing (NGS), while plasma samples were tested with NGS and/or BEAMing Digital PCR, for the first time nationwide.
<b>Results:</b>	Our preliminary results confirm the high concordance of liquid with tissue biopsies and are in agreement with previously reported <i>RAS</i> mutation frequencies. Full data of tumour mutation profile in tissue and plasma, along with their clinicopathological associations, will be presented in the Hellenic national Clinical Oncology Congress.
<b>Conclusions:</b>	The current study endorses the role of liquid biopsies in guiding patients' treatment, contributing to their establishment as prognostic and predictive biomarkers for mCRC in Greece.

# A CASE OF A WOMAN PRESENTING WITH ADVANCED MERKEL CELL CARCINOMA OF UNKNOWN PRIMARY ORIGIN

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**Introduction:** Merkel cell carcinoma is a rare, very aggressive neuroendocrine cutaneous tumor. Its incidence has progressively increased over the past decade. These tumors have a strong tendency to progress locally. It is not uncommon to progress either with distant metastases or locally ( 25-50% ). Patients with advanced unresectable disease are indicated for the use of first-line immunotherapy, with similar response rates to chemotherapy (62% vs 60%).

**Aim:** We will present a case of a woman diagnosed with advanced Merkel cell carcinoma of unknown primary origin. According to the literature, it is not that uncommon for these cancers to present without a known primary origin. Based on older data (prior to the approval of immunotherapy), the first line treatment is chemotherapy.

**Case:** A 60-year old woman presented with abdominal pain and constipation due to which she was subjected to a CT scan and an MRI, which revealed a 10cm mass on the left lateral abdominal wall. On 8/2018 an attempt was made to surgically have a biopsy and excise the disease. During the operation, the mass was found to invade the iliac vessels, the left ureter, left ovary and part of the uterus, and to immobilize the sigmoid colon, and was therefore deemed unresectable. The mass was also fragile and bleeding, and a biopsy was taken. The biopsy revealed a Merkel cell carcinoma. A second-opinion pathology consultation report confirmed the first one, and a PET-CT scan revealed no other lesions. At this point, the mass had grown to 22cm; it displaced the pelvic organs and surrounded the left external iliac artery. Loss of definition of the left iliac vein was also noted on imaging. The patient's lab results were significant for normocytic normochromic anemia, thrombocytosis (669.000) and elevated LDH=1034. The patient herself was in bad general condition (ECOG PS=3). Due to the advanced symptomatic disease, the decision was made to initiate treatment that would have immediate impact, and the patient was started on chemotherapy instead of immunotherapy. On 9/2018, the patient started chemotherapy (cisplatin/Etoposide regimen). Already from the first cycle the patient seemed to be responding to the treatment. Her clinical condition progressively improved (ECOG PS=1), and her LDH levels progressively dropped (LDH=330 after the 2<sup>nd</sup> cycle, LDH=233 after the 3<sup>rd</sup> cycle). During her treatment she presented with hematological toxicity which was attributed to the chemotherapy, and she received blood transfusions as required. After the 4<sup>th</sup> cycle of treatment a new CT scan was ordered and revealed the mass to have been reduced in half (11cm x 7,5 cm), with signs of central necrosis.

**Conclusions:** Even though Merkel cell carcinoma is a type of skin cancer, the above case describes a woman with advanced unresectable disease without a known primary lesion. The patient seemed to be responding to chemotherapy. It should also be noted that in case of relapse, the patient will be suitable for immunotherapy as a second line of treatment.

# PRIMARY PREVENTION OF LUNG CANCER. SMOKING HABITS AND OPINION OF GREEK MEDICAL STUDENTS ABOUT SMOKE-FREE LEGISLATION

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<b>Introduction:</b>	Lung cancer is the most common cause of cancer death for both men and women, even though is the second most common type of cancer for both genders. The prevention on first and secondary level is essential. The most important study factor of the first-level prevention is smoking.
<b>Aim:</b>	The main purpose of this study was the epidemiological analysis of the smoking habits of medical students in Greece, as well as their opinion and thoughts about the anti-smoking laws, in order to underline the importance of rising awareness and applying stricter measures to lessen smoking habits, concerning both active and passive smoking.
<b>Methods:</b>	For this cause, we used the 2013's questionnaire about the implementation of the anti-smoking laws for the public protection from the passive smoking, which was published by the Biomedical Research Foundation Academy of Athens. The questionnaire was filled in online by 302 medical students from four Greek medical schools. The answers received were analyzed in diagrams in order to evaluate the level of sensitization of the future doctors for the protection of the public from the negative effects of smoking, most notably that of lung cancer.
<b>Results:</b>	The main results from this epidemiological study are that the prevalence of smoking in our sample is 24.5% compared to 25.4% of the general population, but those who say they have never smoked are much more (69, 2% vs. 41.2%). A very high proportion of students (94.7%) consider the national target for the reduction of smoking in our country to be quite or very important, while the majority of the sample (82.1%) feels anger about non-compliance with anti-smoking laws.
<b>Conclusions:</b>	The above results leading to the conclusion that students of Greek medical schools seem to be more aware than the general population about the smoking prevention.

# CRANBERRIES AS A SOURCE OF DRUG-LIKE COMPOUNDS WITH ANTICANCER ACTIVITY

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<b>Introduction:</b>	Cancer is the second cause of death worldwide, whose prevalence is increasing. Prevention of cancer and improvement of therapeutic strategies are essential steps for disease management. Dietary modifications can lower the risk of developing cancer, while the past years cranberry's anticancer actions have been investigated.
<b>Aim:</b>	The present study aims to summarize the latest data on the anti-cancer activities of cranberry.
<b>Methods:</b>	PubMed database was searched to identify <i>in vivo</i> και <i>in vitro</i> studies that investigate the role of cranberry and its components against cancer.
<b>Results:</b>	Current <i>in vitro</i> studies have indicated that cranberry and/or its components may act as chemopreventive agents, diminishing the risk for cancer by inhibiting cells oxidation and inflammatory-related processes, while they may also exert chemotherapeutic effects by inhibiting cell proliferation and angiogenesis, inducing cell apoptosis and attenuating the ability of tumour cells to invade and metastasise. Limited <i>in vivo</i> studies have further documented potential anticancer activity. Cranberry could be considered as a conglomeration of potential effective anticancer drug-like compounds.
<b>Conclusions:</b>	Several <i>in vitro</i> and some <i>pilot in vivo</i> studies support the beneficial effect of cranberry and its compounds against cancer. Further studies conducted <i>in vivo</i> and in clinical settings are needed in order to confirm the current promising laboratory and experimental hypotheses and improve the efficacy of current drugs and novel drug-like compounds.

# THE PROGNOSTIC POTENTIAL OF EASILY OBTAINABLE NUTRITIONAL STATUS ASSESSMENT TOOLS IN HEAD AND NECK CANCER PATIENTS

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<b>Introduction:</b>	Head and Neck Cancer (HNC) is the 7th most common cancer type worldwide. At the time of diagnosis, 3–52% of head and neck squamous cell carcinoma (HNSCC) patients are malnourished. During treatment, malnutrition is already present in 44–88% of patients. Various studies have been conducted to evaluate the role of easy-to-obtain measures of nutritional status in HNC cancer patients.
<b>Aim:</b>	This study aims to critically summarize and discuss the currently available clinical data on the efficiency of easily obtainable nutritional status assessment tools, such as weight loss and Bioimpedance analysis (BIA) measures in the evaluation of malnutrition in HNC patients, highlighting on their role to affect disease progression and prognosis.
<b>Methods:</b>	PubMed database was thoroughly searched using relative keywords.
<b>Results:</b>	Current studies investigating the potential of the BIA-derived raw data have shown that phase angle (PA) and Capacitance of the cell membrane may be considered prognostic factors of survival, yet there are contradictory results, concerning the potential of their potential on predicting patients' malnutrition. There is currently inconclusive evidence on weight loss' prognostic impact on survival and post-operative complications, with merely few studies supporting its prognostic value. However, great weight loss >10% has been described as an independent prognostic factor of shorter survival, and treatment failure, while weight loss was associated with treatment toxicity.
<b>Conclusion:</b>	BIA measures can be used as prognostic factors, but currently weight loss does not seem to have prognostic value for HNC patients. Further studies are needed to clarify the role of BIA on the assessment of the patients' nutritional status. Additional high-quality and well-designed studies, which take into account body composition and BMI should be performed to clarify the prognostic role of weight loss in HNC.

# RISK FACTORS TO THE VIOLATION OF MEDICAL CONFIDENTIALITY AT CLINICAL PRACTICE

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<b>Introduction:</b>	Stricto sensu, doctors take the oath Of Hippocrates not to reveal details about the condition of a patient with the exception of a next of kin under a very closed number of certain circumstances and conditions. Medical confidentiality is a very important element of clinical practice and in most cases, violations are taking place deriving from risk factors not yet determined.
<b>Aim:</b>	The present research aims at the medical doctors in Greece and we are searching hospitals and clinics in order to bring to the surface the most important risk factors of the violation of medical confidentiality. We are focusing at the clinical practice breaches since these are the circumstances where doctors should hold their oath to Hippocrates under any pressure. Moreover, our research concentrates in certain aspects of medicine such as decisions that affect the beginning and the end of human life and how important the medical confidentiality is in keeping the human dignity worthy
<b>Methods:</b>	We examined all kinds of clinics with the use of a closed questionnaire which has been filled by clinical physicians at the two major public hospitals in Patras . Nurses and other medical staff were not part of this research due to specific targeting. It has been very important to reveal how the medical confidentiality is violated in different clinics and to discuss over the risk factors which lead a doctor to disclose medical information of a patient.
<b>Results:</b>	In a variety of incidents, doctors perform really well under extreme conditions but sometimes there may be a breach deriving from mistakes in file managing of from physicians-patient affairs. Taking into consideration the new European regulation for the General Data Protection Regulation, which has been mandatory for all European countries since May 25 <sup>th</sup> 2018, very important questions referring to G.D.P.R. have been dedicated in order to find out how well physicians are informed about the new regulations and the penalties that have been undergoing. In most cases, physicians make proper choices according to bioethics and medical instinct and much less by following rules, especially in the field of emergency medicine or at the very end of a patient's life.
<b>Conclusions:</b>	This research will help scientists understand better the way of making a pivotal decision in critical conditions at the clinical practice and enroll seminars and webinars which could help doctors and physicians master very important information about the medical confidentiality, the G.D.P.R. and the legal matters that follow malpractice. A very important factor in confidentiality breach is medical ethics. For many physicians the best call depends on many key factors such as proper education, bioethics and the human factor and it is revealed that infrastructure is less important.

# EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF NAFLD- ASSOCIATED HEPATOCELLULAR CARCINOMA: OUR EXPERIENCE

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**Introduction:** In the last five years, there has been a global increase in the incidence of hepatocellular carcinoma associated with non-alcoholic fatty liver disease (NAFLD), which is further aggravated by the metabolic syndrome epidemic.

**Aim:** The aims of this paper include the study of patients diagnosed with NAFLD-associated HCC, as well as a comparison of their characteristics to HCC patients due to other predisposing factors.

**Methods:** 137 patients were included in total (36 with NAFLD-associated HCC and 101 with HCC due to other liver disease). The two subsets of patients were comparatively studied as to their differences in clinical characteristics [sex, age, presence of cirrhosis, diabetes mellitus (DM), AFP values] and HCC morphology (unifocal or multifocal).

**Results:** Out of 137 patients (116 male, average age of 65.3 years), NAFLD- HCC was confirmed in 36 patients [30 male (83.3%)], average age of 67.2+9.38 years, whereas non-NAFLD- HCC was recorded in 101 patients [86 male (83.3%)], average age of 64.6+9.95 years [p=0.9]. The average value of AFP was 45.564 ng/mL + 655.308 for the NAFLD- HCC group and 28.166 ng/mL + 1.138.528 for the non- NAFLD-HCC group [p=0.6]. Finally, multifocal disease was confirmed in 17% of patients with NAFLD- HCC, versus 35% in the non- NAFLD- HCC group [p<0.05]. 6 out of 36 (16.7%) of NAFLD- HCC patients had no histological signs of cirrhosis and 77% had a DM2 diagnosis.

**Conclusions:** NAFLD-associated HCCs have a statistically significant tendency towards unifocality, compared to non-NAFLD associated HCCs, a third of which are multifocal. In addition, 1 out of 5 cases shows no signs of cirrhosis at time of diagnosis. Given that our knowledge surrounding the pathophysiology and characteristics of this relatively new oncological entity is, at present, incomplete, further studies including a larger sample of patients are needed in order to validate these results.

# THE KENT ONCOLOGY CENTRE CLINICAL AUDIT FOR CARCINOMA OF UNKNOWN PRIMARY (CUP): A TOOL TO IMPROVE CLINICAL PRACTICE?

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<b>Introduction:</b>	Cancer of unknown primary (CUP) is a heterogeneous clinical syndrome with complicated and prolonged diagnostic pathway, representing 3-5% of all malignancies. UK National Institute for Health and Clinical Excellence (NICE), defines three types of CUP: The clinically diagnosed metastatic cancer without histopathological confirmation (malignancy of undefined primary, MUO); the cytologically or histologically confirmed metastatic malignancy following initial investigations (provisional CUP, pCUP); and, the histopathologically confirmed after appropriate specialised investigations (confirmed CUP, cCUP).
<b>Aim:</b>	This retrospective study reviewed the diagnostic pathway and management of patients presenting as CUP in Medway Hospital, Kent, UK, between April 2017 and March 2018. The purpose of the audit was to provide the framework of investigation and subsequent management of patients presenting with MUO. We aimed to improve delays on the diagnostic pathway and subsequent outcomes for both patients who should be treated radically and, those with a poor prognosis who may benefit from palliative care.
<b>Results:</b>	Seventy-three patients presented with MUO. Forty-six primary cancers (63%) were identified, following clinical, radiological and, pathological review, enabling prompt referrals to relevant specialist teams. Histology was not obtained in 11 cases (15%), taken that the results would not influence patients' management. Among the 16 CUP patients (22%), 11 were pCUP (15%), whereas 5 were diagnosed with cCUP (7%), respectively. Three out of the 5 patients with cCUP (60%) received treatment, while the remaining 2 (40%) were treated with palliative care. The overall survival of the cCUP patients was 159 days (ranged 48 to 303).
<b>Conclusions:</b>	Even though, CUP has been recognized as a clinical entity, the incidence of the MUO, pCUP and cCUP subtypes, is still unknown. Differentiation of these subtypes would help clarify the public health burden of the disease. The therapeutic consideration should include treatment for patients presenting with treatable phenotypes and palliative care for those who do not.

# AN AUDIT OF CURRENT PRACTICE AND MANAGEMENT OF METASTATIC SPINAL CORD COMPRESSION AT KENT ONCOLOGY CENTRE: A PRACTICE REFLECTION

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<b>Introduction:</b>	Malignant spinal cord compression (MSCC) is one of the most devastating complications of cancer. This event requires rapid decision making on the part of several specialists, given the risk of permanent spinal cord injury or death. The goals of treatment in spinal metastases are pain control and improvement of neurological function.
<b>Aim:</b>	Our retrospective audit identified 53 patients with suspected MSCC who entered the relevant pathway from April 2017 to March 2018. Our audit standards were set out by our hospitals' MSCC working group members using a combination of published evidence and best practice.
<b>Results:</b>	The patients with suspected MSCC were 53 and, 29 out of them [54.7%] had confirmed MSCC. The most common malignancies within the confirmed MSCC were lung [11 patients, 37.9%], breast [5 patients, 17.2%], and renal [3 patients, 10.3%], followed by prostate, melanoma and, carcinoma of unknown primary [2 patients, (6.9%) each], as well as pancreatic, colorectal, lymphoma and, bladder [1 patient, (3.4%) each]. A magnetic resonance imaging (MRI) scan was performed in 48 patients [90.5%]; the majority [31 patients, 64.6%] underwent the MRI within the first 24 hours, whereas 3 patients had the investigation between 24 and 72 hours from the admission. Among the 29 patients with confirmed MSCC, 6 [20.6%] were treated with surgical decompression, while 20 [69%] received radiotherapy and, 3 [10.3%] best supportive care, respectively. Median time to surgery was 5 days [ranged between 2 and 8 days], whereas for radiotherapy 44.4 hours [ranged between 24 and 72 hours]. Finally, all 3 patients decided for symptoms' control were referred to palliative care team within the first 24 hours following the MRI scan.
<b>Conclusions:</b>	MSCC is frequently presented outside tertiary care. This may cause subsequent delays in investigation, diagnosis and, treatment that can be improved by following a fast track referral pathway.

# DELAYED ONSET PNEUMONITIS IN TWO PATIENTS WITH METASTATIC BREAST CANCER OCCURRING AFTER DISCONTINUATION OF EVEROLIMUS

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**Introduction:** Non-infectious pneumonitis is a potentially life-threatening side effect of the mTOR-inhibitor Everolimus which often leads to discontinuation of the drug.

**Aim:** Description of two patients with metastatic breast cancer who developed delayed pneumonitis few weeks after discontinuation of Everolimus.

**Results:** The first patient presented with symptomatic pneumonitis two weeks after Everolimus discontinuation. She had received a total of 5 months of treatment with Everolimus and Exemestane as second-line treatment for metastatic breast cancer, which was discontinued due to rash, stomatitis and hyperglycemia. Symptoms of pneumonitis included dyspnoea and hypoxemia, while CT scan of the chest revealed diffuse infiltrates, interstitial thickening and pleural effusions. Diagnostic evaluation including BAL bronchoscopy excluded infectious pneumonitis or disease progression, thus confirming the diagnosis of Everolimus-associated grade 3 pneumonitis. Methylprednisolone was administered with clinical and radiological improvement.

The second patient had received Everolimus and Exemestane for 9 months as second-line treatment for breast cancer metastatic to the bones. Everolimus had been discontinued due to disease progression. One month after Everolimus discontinuation, the patient presented with dyspnoea, thoracic pain and hypoxemia. CT scan of the chest revealed infiltrative lesions and pleural effusions. Diagnostic evaluation excluded infectious etiologies or disease progression, and was suggestive of grade 3 pneumonitis due to Everolimus. Methylprednisolone was administered, resulting in symptomatic remission, restoration of respiratory function and imaging improvement.

**Conclusions:** We present two unusual cases of metastatic breast cancer with delayed non-infectious pneumonitis occurring few weeks after Everolimus discontinuation. Thus, all patients should be followed for side effects during as well as post Everolimus treatment.

# TUMOR MUTATIONAL BURDEN (TMB): DETERMINATION, CUT-OFFS AND ITS EMERGING IMPORTANCE IN IMMUNOTHERAPIES

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**Introduction:** Tumor Mutational Burden (TMB) or Load (TML) is an emerging, independent biomarker of outcomes with immunotherapy in multiple tumor types. It is measured as the total number of somatic mutations that exist within a tumor's genome as usually determined by Whole Exome Sequencing (WES). Measurements of TMB (Mutations per megabase (Muts/MB)) from comprehensive gene panels are strongly reflective of measurements from WES and provide a feasible, cost- and time- effective approach in clinical practice. A subset of these mutations may result in an expressed protein, termed neoantigen that is not recognized by the host's immune system as self, and therefore has the potential to be immunogenic, leading to an antitumor immune-mediated response.

**Aim:** The aim of this study was the comparison of TMB values obtained from WES and comprehensive gene panels using TCGA data and the retrospective analysis of results obtained from the application of a 409 gene panel to 200 tumor samples towards the calculation of TMB.

**Methods:** We performed bioinformatics analysis of WES data of 9125 cancer samples from TCGA's Pan-Cancer Atlas, towards the comparison of TMB values obtained from WES and comprehensive gene panels and to compared the different TMB values across 33 cancer types. Moreover, we investigated the determination of clinically relevant cut-offs for the characterization of TMB as high in TCGA samples and clinical trial data obtained from the literature. On a second part, we analyzed 200 tumor samples with a 409 gene panel to determine TMB using Next Generation Sequencing (NGS) with the Ion GeneStudio S5 Prime System (Thermo Fisher Scientific).

**Results:** The Bioinformatics analysis of the samples from TCGA showed that measurements of TMB from comprehensive gene panels have high correlation ( $R^2 \sim 0.98$ ) with measurements from WES. Through the application of the 409 gene panel on 200 tumor samples, we observe a median of 10.2 Muts/MB per sample with different TMB value ranges across cancer types.

**Conclusions:** The determination of TMB can be accessed efficiently from comprehensive gene panels at a lower cost and provide a feasible approach in clinical practice. The characterization of samples as TMB high or low is determined according to the different cancer types in combination to the therapeutic approaches used in clinical trials.

# RECORD OF THE TEN-YEAR OPERATION OF “ALMA ZOIS” HELPLINE: BREAST CANCER PATIENTS’ NEEDS

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**Introduction:** Helpline of Hellenic Association of Women with Breast Cancer “Alma Zois” has been a solid source of information and support for patients with breast cancer (early and metastatic) since 2006. During the 10-year operation, patients’ calling requests are recorded in detail. Requests concern psychological support, information about labor and pension rights and legal counseling.

**Aim:** The aim of this work is to record the most frequent requests of breast cancer patients and to highlight possible differences in these demands among/between patients with early and metastatic breast cancer in Greece.

**Method:** Overall, data from 7,748 patients with early and metastatic breast cancer who asked help from the Helpline from 2007 to 2017 were analyzed to draw conclusions about their needs. The analysis was made using the IBM SPSS Statistics statistical package.

**Conclusions:** Results from data analysis show that the frequency of requests from metastatic breast cancer patients regarding psychological support is increased compared to that of women with early breast cancer ( $\chi^2 = 63.01$ ,  $df = 2$ ,  $p = .000$ ). These results show the importance of dealing with the increased needs of metastatic breast cancer patients and can be used to design targeted programs that will respond more effectively to the needs of different patient groups. In addition, they can help health professionals to understand better their patients’ needs and improve their communication with them.

# PKM2 EXPRESSION AS BIOMARKER FOR RESISTANCE TO OXALIPLATIN-BASED CHEMOTHERAPY IN COLORECTAL CANCER

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**Aim:** To investigate the prognostic significance of PKM2 mRNA expression loss in patients with operable colon cancer (CC).

**Materials and Methods:** Two hundred sixty-two specimens from patients with stage III or high-risk stage II CC (group A), treated with adjuvant fluoropyrimidine and oxaliplatin chemotherapy (ox+FP), 118 specimens from patients with metastatic CC (group B) treated with ox+FP and 104 patients with metastatic CC (group C) treated with irinotecan-based chemotherapy, were analyzed for PKM2, TS, ERCC1, MYC, and NEDD9 mRNA expression, KRAS exon 2 and BRAFV600E mutations.

**Results:** High PKM2 mRNA expression was correlated with left-sided located primaries ( $p=0.001$ , group A;  $p=0.003$ , group B;  $p=0.001$ , group C), high grade tumors ( $p=0.001$ , group A;  $p=0.017$ , group B;  $p=0.021$ , group C), microsatellite stable tumors ( $p<0.001$ , group A) pericolic lymph nodes involvement ( $p=0.018$ , group A), and cMYC mRNA expression ( $p=0.002$ , group A;  $p=0.008$ , group B;  $p=0.006$ , group C). High PKM2 mRNA expression was correlated with significantly lower Disease Free Survival (DFS) [HR: 1.88 (95% ci: 1.37-2.99);  $p=0.002$ ] and Overall Survival (OS) [HR: 1.91 (95% ci: 1.45-2.97);  $p=0.001$ ] in patients' group A. Similarly, PKM2 mRNA expression was associated with significantly decreased Progression Free Survival (PFS) [HR: 1.94 (95% ci: 1.38-3.32);  $p=0.001$ ] and Overall Survival (OS) [HR: 1.99 (95% ci: 1.49-3.41);  $p=0.001$ ] in the group B. In contrary, no significant association for the PKM2 mRNA expression has been observed with either Progression Free Survival (PFS) [HR: 1.08 (95% ci: 0.66-1.69);  $p=0.612$ ] or Overall Survival (OS) [HR: 1.03 (95% ci: 0.59-1.39);  $p=0.517$ ] in group C.

**Conclusions:** The current study provides the evidence for the predictive significance of PKM2 mRNA expression oxaliplatin-based treatment resistance, and the findings merits validation in a larger prospective cohort.

# ACTIONABLE MUTATIONS IN 3084 PATIENTS WITH CANCER: THE HELLENIC COOPERATIVE ONCOLOGY GROUP PRECISION MEDICINE INITIATIVE

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<b>Introduction:</b>	Precision Medicine aims to the personalization of patient management based on tumor molecular alterations in combination with individual patient and tumor characteristics. Tumor molecular profiling enables the identification of actionable mutations that can be used as therapeutic targets.
<b>Aim:</b>	To identify actionable molecular alterations across tumor types.
<b>Methods:</b>	Patients had been referred to Departments of Medical Oncology affiliated with the Hellenic Cooperative Oncology Group. Tumor molecular profiling was performed for research purposes in formalin-fixed paraffin-embedded tumor tissues, obtained from 01/1982 to 12/2017. Gene panels (16-101 genes) comprised of clinically significant genes based on previously published literature. Next-generation sequencing had been performed at the Laboratory of Molecular Oncology (MOL), Hellenic Foundation for Cancer Research, Aristotle University of Thessaloniki. Bioinformatics analysis was performed at MOL, MD Anderson Cancer Center and Victor Chang Cardiac Research Institute, Australia.
<b>Results:</b>	From 2013 to 2017, molecular profiling was successfully performed in 3,084 tumors; breast (1,839 tumors), colorectal (524), pancreatic (187), nasopharyngeal (143), brain (131), gastric (102), biliary (81) and ovarian (77). Overall, 1,529 pathogenic mutations were identified in 21 targetable genes. Actionable mutations were identified in 852 (27.6%) patients; 381 (12.4%) in “highly actionable” genes, associated with US Food and Drug Administration (FDA)-approved therapies; and 552 (17.9%) in genes that “modify treatment options”. Among all patients, 165 (5.4%) patients had pathogenic mutations in $\geq 2$ actionable genes.
<b>Conclusions:</b>	Tumor molecular profiling enables the identification of actionable mutations across tumor types. Prospective validation of the benefits of the implementation of tumor molecular profiling in clinical practice is warranted.

# ASSOCIATION OF VITAMIN D RECEPTOR (VDR) GENE POLYMORPHISMS WITH CANCER DEVELOPMENT AND PROGRESSION IN STAGE II-IV COLORECTAL CANCER PATIENTS

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<b>Introduction:</b>	Vitamin D deficiency has been correlated with high incidence of colorectal cancer (CRC) and high mortality rates. Vitamin D mediates its activation through its binding with the Vitamin D receptor (VDR) of the corresponding gene. Such correlations can be explained following understanding of the VDR gene polymorphisms.
<b>Aim:</b>	The aim of the current study was to investigate the <i>TaqI</i> , <i>Apal</i> , <i>FokI</i> and <i>BsmI</i> polymorphisms of the VDR gene in order to understand their association with CRC development and progression.
<b>Methods:</b>	Peripheral blood was collected from 397 CRC patients (202 stage II/III and 195 stage IV). As control groups, blood samples from 100 healthy donors and tissues from 40 patients with adenomatous polyps were also analyzed. Genotyping of all samples was performed using PCR-RFLP.
<b>Results:</b>	A statistically significant association was revealed between all four VDR polymorphisms and CRC. The highest detection rate of the homozygous mutant alleles (tt, aa, ff or bb) was associated with higher incidence of CRC development ( $p < 0.001$ ). Similarly, the higher detection rate of the homozygous mutant alleles (tt, aa, ff or bb) was significantly associated with the metastatic status (stage IV) ( $p < 0.001$ ) and thus with patients overall survival (OS) ( $p < 0.001$ ). Moreover, all VDR gene polymorphisms analyzed were significantly correlated with KRAS mutations and TLR2, TLR4 and TLR9 gene polymorphisms. Multivariate analysis revealed tt, aa and ff genotypes as independent prognostic factors associated with decreased OS ( $p = 0.001$ , $p < 0.001$ and $p = 0.001$ , respectively).
<b>Conclusions:</b>	The higher detection incidence of VDR gene <i>TaqI</i> , <i>Apal</i> , <i>FokI</i> and <i>BsmI</i> polymorphisms in CRC patients, highlights the role of these polymorphisms in CRC development and progression.

# CELL-FREE DNA INTEGRITY (CFDI) AS A POTENTIAL PROGNOSTIC BIOMARKER IN METASTATIC GASTRIC CANCER PATIENTS

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<b>Introduction:</b>	Cell-free DNA (cfDNA) is a promising biomarker for molecular diagnosis, prognosis and monitoring of treatment response in various types of cancer. An additional feature of cfDNA is its quality, which implies its origin and is represented by DNA Integrity (cfDI: cell-free DNA Integrity). CfDI is the ratio of larger DNA fragments to smaller fragments and indicates the degree of DNA fragmentation. The increased ratio between larger fragments to smaller apoptotic fragments could be a promising marker of detection of the release of cancerous DNA into the bloodstream.
<b>Aim:</b>	The purpose of this study is to measure the integrity of DNA in 50 samples of cfDNA in patients with metastatic gastric cancer and in 50 samples of healthy donors, in order to investigate its prognostic and predictive value.
<b>Methods:</b>	The cfDI calculation was performed with qReal Time PCR for the recurring ALU sequences, namely ALU115 and ALU247. Initially, a reference curve was performed for both primer pairs, which consists of successive decimal dilutions of DNA of known concentration (100ng, 10ng, 1ng, 0.1ng, 0.01ng). The quantification of the DNA samples was performed using the corresponding reference curve. The ratio ALU247 / ALU115 was then calculated.
<b>Results:</b>	As a result, cfDI is significantly higher in samples of metastatic gastric cancer (mean values: 0.51) than in healthy donors (mean values: 0.27). Based on the survival analysis, it seems that patients with low cfDI have a higher OS, compared to patients with high cfDI.
<b>Conclusions:</b>	CfDI is a potential prognostic biomarker for patients with metastatic gastric cancer. Whether cfDI could be a predictive biomarker, will be a further subject of our research.

# DETECTION AND CLINICAL EVALUATION OF TUMOR SUPPRESSOR GENES METHYLATION IN CELL-FREE DNA (CF-DNA) OF METASTATIC GASTRIC CANCER PATIENTS

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<b>Introduction:</b>	The relationship between DNA methylation and cancer is the subject of intensive research, in order new molecular markers to be detected. Hypermethylation markers can be used to detect primary tumor, relapse, metastasis, and patient response to treatment. In particular, in metastatic disease, the identification of methylation biomarkers, as features of malignant transformation and metastasis, may be indicative of more intensive investigation or more regular follow-up.
<b>Aim:</b>	The purpose of this study is to detect the methylation of the <i>RASSF1A</i> , <i>SOX17</i> and <i>WIF-1</i> tumor suppressor genes in the cfDNA of patients with metastatic gastric cancer (n = 55). A further objective of the study is to determine the concentration of plasma cfDNA in these patients.
<b>Methods:</b>	QUBIT and real-time PCR, specific for the recurrent ALU sequences was used and a comparison of the two above methodologies and the correlation of the concentration of cfDNA with clinicopathological characteristics of the patients was performed.
<b>Results:</b>	<i>RASSF1A</i> , <i>SOX17</i> and <i>WIF-1</i> genes were found to be hypermethylated in the cfDNA of the patients at 76.3%, 63.6%, and 54.5%, respectively. Survival analysis followed, where patients with unmethylated <i>SOX17</i> and <i>WIF-1</i> genes were found to have a higher disease free survival (DFS) than those who had the above genes methylated (p = 0.001 and p = 0.043, respectively). Also, overall survival (OS) was higher for patients with unmethylated <i>SOX17</i> and <i>WIF1</i> genes (p = 0.001 and p = 0.027, respectively). Clinical evaluation of the cfDNA concentration indicates that patients with a high cfDNA concentration ( $\geq 0.5$ ng/ $\mu$ l) exhibit a lower DFS.
<b>Conclusions:</b>	Hypermethylation of tumor suppressor genes is an early event in carcinogenesis and remains during metastatic transformation. Methylation of the above genes appears to be a good prognostic biomarker, but its value should be validated and confirmed in an even larger number of patients.

# SALVAGE RADIOTHERAPY TREATMENT AFTER RADICAL PROSTATECTOMY TO PATIENTS WITH PSA<0.5ng/ml AND THE INFLUENCE TO POSTTREATMENT PSA AS TO DISEASE PROGRESSION.THE EXPERIENCE OF OUR DEPARTMENT

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<b>Introduction:</b>	Salvage Radiation Therapy(RT) is the treatment of choice for biochemical recurrence after radical prostatectomy. Biochemical recurrence is determined as the rising of PSA to $\geq 0.2$ ng/mL which is confirmed and with a second measurement.
<b>Aim:</b>	Our purpose was to evaluate retrospectively the influence of salvage RT, to patients with biochemical recurrence - PSA ranging from $\geq 0.2$ ng/ml to 0.5ng/ml, to post treatment PSA as also to disease progression.
<b>Methods:</b>	From 2010 to 2016 twenty five patients were treated (salvageRT) to our department for biochemical recurrence with PSA ranging from to PSA $\geq 0.2$ ng/ml to <0.5ng/ml (median PSA:0.23ng/ml range 0.2-0.41ng/ml).Patients that had receive hormone therapy with LHRH where not included in the study. All patients had undetectable PSA(<0.1ng/ml) after radical prostatectomy. According to histological reports all surgical margins were negative. Median follow-up was 38 months. The planning for Radiation Therapy treatment was 3D-conformal (3D-CRT) and total dose delivered, was 66Gy ,2Gy/per fraction for all patients.
<b>Results:</b>	After salvage RT eighteen patients (72%) recovered undetectable PSA:<0.1ng/ml. For 4patients (16%) PSA remained to levels from>0.1ng/ml to $\geq 0.2$ ng/ml. Nadir posttreatment PSA for 2 patients (8%) remained to levels>0.2ng/ml. One patient (4%) was not amenable to posttreatment follow-up. To retrospective analysis PSA $\geq 10$ ng/ml before radical prostatectomy, pathological stage,pT3, Gleason score (GS) 7-10),PSA > 0.2ng/ml before salvage RT and nadir PSA after salvage RT $\geq 0.1$ ng/ml were negative correlated with disease progression.
<b>Conclusions:</b>	In prostate cancer salvage RT after radical prostatectomy may recover undetectable levels of PSA:<0.1ng/ml offering to patients a second chance. Our results are similar to those of international bibliography. Evidenced based data from more trials are necessary to establish whether salvage RT with PSA $\geq 0.1$ ng/ml will offer substantial benefit to certain groups of patients.

# SMALL CELL BLADDER CARCINOMA –A RARE TUMOR

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<b>Introduction:</b>	Small cell bladder carcinoma is a very rare tumor(only 0.7% of bladder tumors)with an aggressive behavior and a poor prognosis.It belong to poorly differentiated neuroendocrine carcinoma.(NETs).
<b>Aim:</b>	The aim of our study is to describe the experience of our department in this tumor.
<b>Methods:</b>	From 2010 to 2017 only three patients with small cell bladder carcinoma were treated in our department .Two were male and one female Mean age at time of diagnosis is 64 years .In the TNM classification all the tumors were T2N2 with invasion of the muscularis propria and multiple regional lymph node in the iliac(stage IIIb).The tumors were poorly differentiated with a Ki-67 proliferative index >40. The most expressed immunohistochemical markers were neuron-specific enolase (NSE) 80%, serotonin 78%, synaptophysin 89% and CD56 77%. All the patients received 3-6 cycle of chemotherapy with cisplatin-etoposide o ifosfamide-doxorybicin and 3-d conformal radiotherapy . The total dose of radiation was 54Gy.All the patients complete the treatment.
<b>Results:</b>	After two years of follow-up two patients were dead(2- year survival 33%) and one had recurrence and was treated with second line chemotherapy.
<b>Conclusions:</b>	Small cell bladder carcinoma is a very rare tumor highly aggressive and with poor prognosis ,mainly in advanced disease(stage III) in which the 2- year survival rates is 33% and the 5-year survival rates is 12% based on the published scientific literature .In conclusion our study accord with the published literature that involves a very small number of patients.

# THE ROLE OF SYSTEMIC INFLAMMATION AND HISTOLOGIC GRADE IN NON SMALL CELL LUNG CANCER (NSCLC)

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**Introduction:** Tumor grade is an important factor of cancer outcome. Systematic inflammation has been associated with tumorigenesis and tumor aggressiveness and prognosis in several human malignancies. Cancer cells create an inflammatory peritumoral microenvironment by releasing a number of cytokines.

**Methods:** In total, 100 patients (88 males) with histologically proven NSCLC and no signs of active infection were evaluated. Tumor grade was examined and systematic inflammatory response was assessed by circulating levels of C-reactive protein (CRP), albumin, ferritin, transferrin and the modified Glasgow Prognostic Score (mGPS). Patients were followed up and survival data were subsequently collected. Associations with clinicopathological, histological parameters and patients' survival were studied.

**Results:** Histological grade was associated with tumor size, the presence of pathological lymph nodes, organ metastases and advanced disease stage ( $p=0.010$ ,  $p<0.001$ ,  $p<0.001$  and  $p<0.001$ , respectively). There was a trend of higher histological grade in adenocarcinomas compared to squamous carcinomas ( $p=0.263$ ). High tumor histological grade was also significantly associated with elevated serum CRP levels ( $p<0.001$ ), hypoalbuminemia ( $p=0.009$ ), elevated ferritin levels ( $p=0.049$ ), abnormal mGPS ( $p=0.006$ ) and a trend for reduced transferrin levels ( $p=0.101$ ). In multivariate analysis, histological grade, stage, ECOG performance status and mGPS were identified as independent prognostic factors for overall survival (Cox regression analysis,  $p=0.002$ ,  $p=0.001$ ,  $p=0.010$  and  $p=0.019$ , respectively).

**Conclusions:** Our data support the association of tumour grade with the presence of systemic inflammation; two well described negative prognostic factors for NSCLC. To our knowledge this is the first time that these factors are associated with each other giving more information about the prognosis in patients with NSCLC.

# EDUCATION AND CAREER DEVELOPMENT IN WEB-ERA: A EUROPEAN SURVEY CONDUCTED BY THE HELLENIC GROUP OF YOUNG ONCOLOGISTS (HeGYO)

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*On behalf of the Hellenic Group of Young Oncologists (HeGYO, <http://www.hesmo.gr/en/gyon/group>), under the auspices of the Hellenic Society of Medical Oncology (HeSMO, <http://www.hesmo.gr/en>) Athens, Greece.*

<b>Introduction:</b>	New technologies, especially internet, promote not only cancer research but also education and career development. The aim of this study was to reveal if European oncologists are familiar and satisfied with these new technologies in the current Web-Era.
<b>Methods:</b>	Residents and specialized medical, clinical and surgical oncologists from Europe were invited to complete a comprehensive forty multiple-choice web-questionnaire. The study was kindly endorsed by scientific organizations such as ESMO YOC, ECCO, ESO and HeSMO.
<b>Results:</b>	These are the final results from 234 participants (61% males). 70% are from Greece and 30% from 16 other European countries. 57.3% are 30-40 years old, 67.5% are medical oncologists while 37.2% are residents. 59.8% are ESMO and 30.3% ASCO members. 28.6% have ESMO accreditation, 30.3% GCP and 32.9% PhD degree. 44% of the responders tend to attend 1-3 national congresses and 70.5% 1-3 international congresses per year which they find beneficial for their continuous education (94%). More than 50% consider ASCO and ESMO website/newsletters useful. The more useful sections of ESMO "OncologyPro" are considered the "Guidelines and Practice" (66%) and the "Oncology news" (49%). Nearly 50% have participated in ESMO fellowships/educational activities and 50% are planning to participate in some of them. 39% of oncologists are satisfied with ESMO fellowships and 83% are satisfied with ESMO educational activities. 55% use LinkedIn, 42% ResearchGate, 18% Facebook and 7% Twitter, while 15% have their own Personal website. For search engine 28% use GoogleScholar, 14% PubFacts and 15% SlideShare. Lack of time and financial issues are considered as the main problems for continuous professional development while clinical practice and on-line medical resources are considered the most effective ways to achieve continuous medical education.
<b>Conclusions:</b>	The majority of oncologists are well informed about the educational opportunities in their countries and in Europe. An increasing number of oncologists gets familiar and satisfied with the new technologies in the Web-Era and use them for their continuous oncology education and career development.

# MEDICAL AND RADIATION ONCOLOGISTS: ARE THERE ANY DIFFERENCES REGARDING EDUCATION OR CAREER AND DEVELOPMENT? A EUROPEAN SURVEY CONDUCTED BY THE HELLENIC GROUP OF YOUNG ONCOLOGISTS (HeGYO)

Aravantinou-Fatorou E., Papaxoinis G., Kamposioras K., Korogiannos A., Papadopoulos V., Lazaridis G., Nikolaou M., Voulgaris E., Bournakis E., Tsigaridas K., Lontos M., Tsapakidis K., Mitsimponas N., Binas I., Litos I., Pantavou E., Papageorgiou E., Chatzifoti N., Varthalitis I., Athanasiadis A., Tsoukalas N.

*On behalf of the Hellenic Group of Young Oncologists (HeGYO, <http://www.hesmo.gr/en/gyon/group>), under the auspices of the Hellenic Society of Medical Oncology (HeSMO, <http://www.hesmo.gr/en>) Athens, Greece.*

<b>Introduction:</b>	Advances in Oncology research and the increasing knowledge of cancer therapeutics render continuous education an absolute necessity for oncologists. Aim of this study was to reveal any differences between Medical and Clinical Oncologists in educational opportunities and continuous professional development.
<b>Methods:</b>	Residents and specialized medical (MedOncs) and clinical oncologists (ClinOncs) from Europe were invited to complete a comprehensive forty multiple-choice web-questionnaire between February 2015 and January 2016. The study was kindly endorsed by scientific organizations such as ESMO YOC, ECCO, ESO and HeSMO.
<b>Results:</b>	These are the final results of a subanalysis from 226 participants. (69% MedOncs, 31% ClinOncs). More MedOncs compared to ClinOncs choose their specialty because they consider it challenging and more available for training (85.3 vs. 68.6%, $p=0.006$ and 22.9 vs. 10.9%, $p=0.025$ respectively). MedOncs reported being more frequently completely satisfied (19.2 vs. 14.3%) and satisfied (35.3 vs. 24.3%) with the accordance of their training to the global curriculum ( $p=0.002$ ). More ClinOncs compared to MedOncs are completely satisfied from the academic tasks and opportunities provided by their National Oncology Society (24.3 vs. 11.5%, $p=0.011$ ). MedOncs reported higher participation in scientific activities such as co-authoring in a medical book (43.6 vs. 22.9%, $p=0.003$ ), participating in an Editorial Board (18.6 vs. 7.1, $p=0.027$ ), giving lectures in congresses (53.2 vs. 24.3%, $p<0.001$ ), participating in translational research (41.0 vs. 25.7%, $p=0.036$ ), in clinical trials (64.7 vs. 44.3%, $p=0.005$ ), or in fellowships (32.1 vs. 18.6%, $p=0.038$ ).
<b>Conclusions:</b>	It is apparent that oncologists are highly thriving for education. More educational activities and career opportunities should be offered for both Medical and Clinical Oncologists. The differences highlighted in this survey need to be validated in a bigger cohort of oncologists.

# CANCER ASSOCIATED THROMBOSIS (CAT) AND ITS CLINICAL MANAGEMENT IN GREECE

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**Introduction:** Cancer has multiple processes that increase thrombogenicity. Thrombosis is the 2nd cause of death in cancer patients. CAT is common, could delay anti-cancer therapy and increase costs. Oncologists should be aware of CAT and its clinical significance.

**Methods:** A prospective observational study conducted by HeSMO in Greek Oncology units, for 1 year, aiming to record CAT clinical management and to identify possible risk factors. Patients with active cancer received antithrombotic agents for treatment or thromboprophylaxis were enrolled, after signing informed consent.

**Results:** In total, 546 patients enrolled from 18 oncology units. Primary cancers were: lung 24%, pancreas 13.4%, breast 8.8%, colorectal 8.1%, stomach 8.1%, ovarian 6.6% and other 39.1%. 120 patients received Low Molecular Weight Heparin (LMWH) for Venous ThromboEmbolism (VTE) treatment (Group A), 426 for thromboprophylaxis (Group B) while no one received oral agents.  
*Group A:* 35% of 120 VTEs were diagnosed incidentally and treated as symptomatic [mean duration 5.51 months (SD+/-3.42)]. Recurrences occurred in 3 (2.5%) patients. Four (3%) patients experienced a grade 1 bleeding.  
*Group B:* 213 (50%) patients received LMWH at prophylactic doses while the rest received therapeutic doses [mean duration 4.42 months (SD +/- 2.68)]. 126 (30%) patients had Khorana score  $\geq 3$ . Even though, 300 (70%) patients had Khorana score  $\leq 2$ , 68% were metastatic and 58% were receiving High Thrombotic Chemotherapy Agents (HTCA, e.g. platinum, 5-FU, gemcitabine). 16 (3.8%) patients experienced VTE while 9 (56%) of them were incidental. Notably, lower VTE risk [OR: 0.32 (95% CI 0.10, 1.0)  $p=0.04$ ] was observed in patients on therapeutic doses LMWH while higher VTE risk [OR: 3,14 (1.01, 9.9)] was observed in patients on prophylactic doses LMWH. Six (1.4%) grade 1 bleedings were recorded.

**Conclusions:** Oncologists use LMWH for the CAT management. Incidental VTE is a common and insidious clinical entity. Therapeutic doses of LMWH for thromboprophylaxis are effective and safe. Although Khorana score is a useful model for CAT risk assessment, some other factors such as disease stage and HTCA might be taken into consideration.

# PRIMARY BONE LYMPHOMA IN A PATIENT WITH MULTIPLE BONE METASTASES

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<b>Introduction:</b>	Primary lymphoma of bone is a very rare malignant disease, which it shows up in most of the cases (>92%) in patients with age older than 30 years. The incidence of the disease is slightly higher in male patients and has better prognosis than the other malignant diseases of the bones.
<b>Case report:</b>	A female, 58 years old, with unremarkable past medical history, presented with gradually worsening chest pain and pain on the left humerus for the last 2 months. She underwent a full cardiology control which came back negative and excluded any cardiac disease. On the CT Scan of the chest, it was showed multiple lytic fractions, on the left humerus, sternum and the body of T2 vertebrae. CT Scan abdomen and pelvis was negative for any pathologic findings and the bone scan confirmed the pathologic findings on left humerus, sternum and T2 vertebrae. Patient was admitted in our hospital, department of internal medicine. First thought in the differential diagnosis was breast cancer, which was later excluded. Furthermore, during the admission, she presented with pathologic fracture of the left humerus and she underwent a surgical restoration of the fracture and at the same time a biopsy was collected to identify the primary cause histologically. Pathology revealed a non-Hodgkin lymphoma (NHL) and in particular a primary NHL of bone. Consequently, patient received 1 <sup>st</sup> line chemotherapy with excellent response in an experienced Haematology department.
<b>Conclusions:</b>	Primary lymphoma of bone consists in a rare malignant disease which affects mainly patients under age of 30-40, mostly male patients and has better prognosis from the rest of malignant diseases of bone and the diagnosis premises the absence of lymphatic or visceral disease.

# METASTATIC EOSOPHAGEAL CARCINOMA AND ACUTE RENAL FAILURE CONTINUING CHEMOTHERAPY ALONG WITH TARGETED TREATMENT

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<b>Introduction:</b>	The incidence of esophageal carcinoma in Western Europe is 5-10 cases/1000 male patients. Adenocarcinoma is the most frequent histological type of this type of carcinoma and it is correlated with reflux esophagitis and obesity. Acute renal failure, which means the acute loss of normal renal function, is a disease which demands urgent medical intervention, mainly treating the cause which provoked the renal failure.
<b>Case report:</b>	Male 60 years old, presented with dysphagia. During the investigations to find the cause of this symptom, a revealing mass was found at the gastroesophageal junction. Histology showed adenocarcinoma high grade. CT scans of chest and abdomen was negative for metastatic disease and the patient proceeded with partial esophagectomy. On CT scans after surgery, multiple hepatic lesions were found and we confirmed that with biopsy of one of the lesions. Furthermore, a PET-CT Scan was performed and showed up positive lymph nodes in the left supraclavicular fossa as well as lymph nodes in the area of upper abdomen and multiple hepatic lesions. Patient underwent 8 cycles of 1 <sup>st</sup> line chemotherapy with Cisplatin and Capecitabine with good partial response. One year later, another PET-CT Scan was performed which showed progression disease of the subcarinal lymph nodes and lymph nodes around the liver and again multiple hepatic lesions. In addition, patient presented with severe acute renal failure, creatinine level=6.1, creatinine clearance= 9 (stage 5 kidney disease), without any evident post renal cause or obstruction which may justify the renal failure. Creatinine levels were not improved after hydration. Because of the large progression of disease, we decided to treat the patient with 2 <sup>nd</sup> line treatment with the combination of Ramucirumab every 2 weeks and Paclitaxel weekly, following the international guidelines. According to Spc, there are no studies for patients with acute renal failure who received this combination of treatment. Clinical data suggest that there is no need of modifying the dose in mild, moderate or severe renal failure. Our patient received 6 cycles in total with the combination. During treatment, renal failure was constantly improved and creatinine came back up to normal levels (1.2) and creatinine clearance=65.
<b>Conclusions:</b>	Metastatic adenocarcinoma of gastroesophageal junction has very poor prognosis. Its treatment becomes even more difficult with simultaneous severe acute renal failure. In our case report, despite the lack of clinical studies on similar cases, it was noted the improvement of renal function during the treatment with Ramucirumab and Paclitaxel. The mechanism remains unknown because of lack of clinical studies.

# METASTATIC COLORECTAL CANCER WITH EXCELLENT RESPONSE TO TREATMENT AND LONG-TERM SURVIVAL

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<b>Introduction:</b>	The incidence of colorectal cancer is increased during the last few years. The treatment of metastatic disease has improved and depends on the molecular profile of the cancer, on the load and the expanse of the disease. The oligometastatic disease on colorectal cancer needs special evaluation and management.
<b>Case report:</b>	Male 58 years old, with PSO, underwent an urgent laparotomy- sigmoidectomy (03/2012) because of acute abdominal pain and in particular because of perforation of sigmoid colon. His past medical history was unremarkable, except from bleeding stools during the last year. Histology revealed adenocarcinoma of colon, high grade, with infiltration of 1 of the 30 lymph nodes removed, focal infiltration of vessels and large infiltration of the nerves. Surgical limits were clear. Kras analysis was negative for mutations (kras wild type). CT Scans showed multiple hepatic lesions and the final stage was T4bN1M1, stage IV. In 05/2012, he started on 1 <sup>st</sup> line chemotherapy with Panitumumab and Folfex, with very good tolerance, except from grade 2 myelotoxicity and grade 2 skin rash on the face and body. CT Scans showed very good response with the conversion of the hepatic lesions from non-operable to operable, since there were just 3 lesions on the left hepatic lobe, a lot smaller than the original ones. In 11/2012 he underwent metastasectomy of the liver lesions and remained under follow up for 7 months. In 06/2013 presented with progression disease on the liver lesions and started on 2 <sup>nd</sup> line chemotherapy with Panitumumab and Folfiri, again with very good tolerance and again grade 2 myelotoxicity, grade 2 skin rash on the face and body and grade 1 diarrhoea, and good partial response on the disease. In 10/2013 two new liver lesions were showed up and he underwent stereotactic radiotherapy with success. He remained on follow up for another 8 months. In 06/2014 presented with solitary lung lesion and complete response on the liver lesions. He refused the surgical excision of the lesion and then stereotactic radiotherapy with success. Since then he remains under follow up, with PSO and without any clear evidence of disease on the CT Scans. In total, our patient presents until today, overall survival 83 months and with excellent quality of life.
<b>Conclusions:</b>	The best management on colorectal cancer should be based on multidisciplinary approach of the patient with the aim of using our therapeutic options in the best possible sequence. The management of oligometastatic disease remains a challenge and it should be examined for each and every patient.