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Letter from **FCO Editors**

Dear Colleagues,

The Hellenic Society of Medical Oncology (HeSMO) decided to publish the accepted abstracts for its annual Congress in a supplementary issue of our scientific journal, Forum of Clinical Oncology (FCO). This was a pivotal decision, highlighting the important role of FCO in promoting the scientific activity of the society. Hopefully, this relationship will be further reinforced and such issues will accompany all future HeSMO congresses as well. In this issue there are accepted abstracts for the 5th Hellenic Congress of Oncology (5th HCO), "Από τους Χειμάρρους των Πληροφοριών στην Κοίτη της Πράξης".

However, it should be noted that this was accomplished only due to the significant contribution of scientists from several disciplines related to oncology. All have shared their important work for the conference and also accepted the challenge to publish their abstracts in this supplementary FCO issue, despite the significant time limitations and the additional required workload. We are really thankful and we hope that this publication will further enhance the dissemination of their work.

Since FCO was launched in 2010, as well as during its previous era under the Greek title "Βήμα Κλινικής Ογκολογίας" eminent Greek Medical Oncologists have successfully led this publication attempt of HeSMO. Concomitantly with this supplementary issue, a new issue of FCO will be released. We hope that these two new releases could successfully continue the tradition built so far.

Yours sincerely,

Editors in Chief

Michalis Liontos Nikolaos Tsoukalas

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Dear Colleagues,

We are writing on behalf of the Editorial Board of **Forum of Clinical Oncology (FCO)**, to introduce you the official scientific journal of the Hellenic Society of Medical Oncology (HeSMO, www.hesmo.gr/en) and to invite you to submit your work to our journal FCO.

FCO (Online ISSN: 1792-362X, https://content.sciendo.com/view/journals/fco/fcooverview.xml) is a web based, open access, peer-review journal launched in 2010, published quarterly. In fact, it was the evolution of the previous official journal of HeSMO entitled "Βήμα Κλινικής Ογκολογίας" that was published in Greek since 1997.

FCO publishes articles in the field of Oncology providing current and practical information on prevention, diagnosis and treatment of all neoplasms. Article types of original research articles, state-of-the-art review articles, short communications, case reports, interesting oncology images, perspectives, editorials and commentaries relevant to oncology clinical practice and basic research are included. Furthermore, FCO also does not charge the authors for article process fee or publication fee.

FCO is currently indexed by many well known databases (for instance Google Scholar, Publons, SCOPUS, etc.) and we hope that it will be indexed by PubMed soon. Previous issues of FCO (2010-2014) can be found at the official site of HeSMO (www.hesmo.gr).

FCO serves as a Forum for communication, presentation of clinical or research data and exchange of thoughts and ideas, reflecting the ongoing efforts of physicians and scientists in Greece, in Mediterranean area and worldwide to improve our clinical practice in Clinical Oncology.

Therefore, we would like to kindly invite all healthcare professionals to submit manuscript for publication to **Forum of Clinical Oncology (FCO)** making this journal an interactive educational tool to acquire knowledge, addressed to all scientists working in Oncology field. Moreover, we are willing to discuss your own suggestions and thoughts.

Your contribution in the journal FCO will be of great importance with your research interest focusing on Oncology. We sincerely hope to have a chance to work with you and make the journal a robust platform for investigators in our field.

Yours sincerely,

Editors in Chief

Michalis Liontos Nikolaos Tsoukalas

5th Hellenic Oncology Conference (9-11 July 2020)

The first entirely web-based national conference.

The 5th Hellenic Oncology Conference, which had to be postponed due to the SARS-Cov2 epidemic, was finally completed in the summer of 2020 and it will surely be unforgettable for many reasons. Firstly, it took place entirely online. What does this mean; Virtually all presentations were videotaped in advance, with the presidents connected in real time to coordinate the discussion and entertain questions while speakers were requested to be available at the time of the presentation of their talk. This was the first major national oncology event in Greece organized in that manner. We can surely say that the whole endeavor was successful, both from a technical point of view and for the high quality of presentations, but also in terms of the number of remote participants that exceeded 800.

Let us recall that it was jointly organized by the Hellenic Society of Medical Oncology and the Hellenic Society of Radiation Oncology, in collaboration with the Associations of Surgical Oncology, Pathological Anatomy and the Oncology Nursing sector of the National Association of Nurses of Greece. The very motto of the conference "From the Torrents of Information to the Riverbed of Clinical Practice" gave the tone and style of the conference that honored the collaborative nature of the practice of oncology and paid tribute to pragmatic oncology which is grounded in the reality of daily practice. For this reason, the conference included many practical topics such as the very successful round tables organized by the Young Oncologists of HeGYO and were related to practical and specific questions related to immuno-oncology. We were really proud of the youngest generation of colleagues whose discussions attained high standards, allowing optimism for the future of oncology in Greece.

The official conference was preceded, as usually, by a whole day of industry-sponsored presentations offered by reputable colleagues, also very helpful and informative. The main conference was characterized by the intention to address most issues related to the practice of oncology at large, the character and soul of oncology we could say, such as the upgrading of oncology centers, the ever-lurking syndrome of burnout, the requirements

for an effective model much needed palliative care and the deficiencies thereoff, concerns about guidelines and regulatory models of new drug approval administration and such. The need for a good cooperation between oncologists and radiation oncologists, cooperation that is necessary for achieving the best outcomes, was again stressed. In Greece, we are in the happy position to say that such a model of gracious interactions has been forged by the good and personal relations between members of these two specialties. Common strive for optimal oncological outcome constitutes the basis of this commendable relationship. Round tables related to collective management of gastrointestinal tumors or prostate cancer served as examples, aiming at demonstrating the importance of inter-specialty communication.

In the context of global and multinational collaboration and exchange of information, the round tables organized in collaboration with the European companies ESMO and ESTRO were of particular importance. Several more foreign speakers participated such as Prof. Ascierto who successfully addressed issues related to the use of ICTs, while Johns Hopkins Professor Dr Makary began his talk by discussing the changes in mentality and practice due to the pandemic. At the end of his talk he presented the "Cancer Expert Network", a free consulting service for oncologists provided in Greece through HeSMO. Hence, there is no doubt that the 5th Hellenic Oncology Conference was a dense, collaborative, useful, multifaceted, realistic, holistic, enlightening, different and interesting conference, which suggests the directions of the future. It was really worth attending for anyone related to the treatment of cancer.

What can be said about this novel format of conferences? It is true that the plentiful of audience questions, debates and controversies were lacking. We had been accustomed to such face-to-face interactions which often were more important than the lectures themselves. Although the current format enabled questions from the audience to be posed electronically, it is true that the distancing was not conducive to audience participation and there was paucity of interaction, partially covered by the discussion among chairpersons and speakers. It is true that the chairs did a great job trying to enrich the discussions, undertaking themselves the duty to address key questions to the speakers, thus acting as representatives of the public who were perhaps hesitant or unfamiliar with asking through the online platform. On the other hand, it is perhaps a good mental exercise to just listen and think in private about the information provided by the erudite speakers. All activities of the conference were posted on the LiveMed platform (https://www.livemed.gr) from where everyone can watch them at ease, at any time.

What does the future hold? We got the first experience of a large-scale webinar. We are still on the ascending part of the learning curve. The experience was useful, but we certainly lacked the immediacy of the live communication. We will probably remain with internet-based conferences, at least for the immediate few months However, the times are constantly changing and this new experience will definitely influence us and what is to come. Hybrid conferences will probably be the way to go, as more people become familiarized with attending via internet. Maybe in the future we will successfully encompass the good of both worlds, physical interaction and real-time electronic dissemination of information. Fare forward travelers!

With kind regards

The Presidents of the Organizing Committee

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Medical Oncologist

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Radiation Oncologist

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UMI-NGS FOR THE ANALYSIS OF LIQUID BIOPSIES IN NSCLC PATIENTS

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Introduction: Analysis of circulating tumor nucleic acids in plasma of Non-Small Cell Lung Cancer (NSCLC) patients is the most widespread and documented form of "liquid biopsy" and provides real-time information on the molecular profile of the tumor without an invasive tissue biopsy.

Aim: The aim of this study was to investigate the feasibility of ctNA analysis in everyday practice, using a sensitive NGS approach in patients with NSCLC. The plasma mutation distribution was calculated in newly diagnosed patients as well as in patients at progression on treatment with EGFR TKIs.

Methods: Liquid biopsy analysis was requested by the referral physician in 121 NSCLC patients at diagnosis and was performed using a sensitive Next Generation Sequencing assay. Additionally, a comparative analysis of NSCLC patients at relapse following EGFR Tyrosine Kinase Inhibitor (TKIs) treatment was performed in 50 patients by both the cobas and NGS platforms.

Results: At least one mutation was identified in almost 49% of the cases by the NGS approach in NSCLC patients analyzed at diagnosis. In 36 cases with paired tissue available a high concordance of 86.11% was observed for clinically relevant mutations, with a Positive Predictive Value (PPV) of 88.89%. Furthermore, a concordance rate of 82% between cobas and the NGS approach for the EGFR sensitizing mutations (in exons 18, 19, 21) was observed in patients with acquired resistance to EGFR TKIs, while this concordance was 94% for the p.T790M mutation, with NGS being able to detect this mutation in three 3 additional patients.

Conclusions: This study indicates the feasibility of circulating tumor nucleic acids (ctNA) analysis as a tumor biopsy surrogate in clinical practice for NSCLC personalized treatment decision making. The use of new sensitive NGS techniques can reliably detect tumor-derived mutations in liquid biopsy and provide clinically relevant information both before and after targeted treatment in patients with NSCLC. Thus, it could aid physicians in treatment decision making in clinical practice.

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EPIDEMIOLOGICAL FEATURES OF PATIENTS WITH NEUROENDOCRINE NEOPLASMS (NENs): PRELIMINARY RESULTS OF AN OBSERVATIONAL STUDY BY THE HELLENIC SOCIETY OF MEDICAL ONCOLOGY (HeSMO)

Koumarianou A., Tsoukalas N., Syrigos K., Demiri S., Ziras N., Kampoli K., Ntavatzikos A., Evangelou,I. Binas G., Stergiou E., Papafilli A., Tzouda V., Sarikaki K., Karadimou A., Kamposioras K., Souglakos I., Athanasiadis A., Varthalitis I., Georgoulias V., Boukovinas I.

On behalf of the Hellenic Society of Medical Oncology (HeSMO, http://www.hesmo.gr/en), Athens, Greece

Introduction: NENs are rare tumors and can grow in almost all tissues. Regardlesshistological, molecular and imaging characteristicsthat are indicative of the primary origin, a significant percentage remain of unknownprimary.

Methods: A prospective observational study was conducted by HeSMOin Oncology Departments to register patients with histologically confirmed NEN. Inclusion criteria were: a) residencyin Greece, b) treatment by medical Oncologist in Greece, c) Age > 14 years and d) signed informed consent.

Results: 169 patients (pts) diagnosed with NENswere enrolledof 6 centers from 1/2012to 12/2018. The female to maleratio (90/79) was 1.1 and the age range was 19-89 years (ys). The higher incidence concerned the age range 60-69 ys(30.1%; 51 pts), followed by 70-79 ys(21.8%; 37pts) and 50-59 ys(20.7%; 35pts). The most frequently primary sites were lung (28.4%; 48 pts), pancreas (15.95%;27pts) and stomach (15.38%; 26 pts). Less frequent were ileum/small intestine (6.5%;11 pts), cecum (4.73%; 8pts), colon (2.36%; 4pts), rectum (1.77%; 3pts) and duodenum (0.6%; 1pt). Less common primary sites were in 20.11% (34 pts) whereasin4.13% (7pts) they wereunknown primary tumors. The distribution of stagesat diagnosis, were early stage in 20%, locally advanced in 48% and metastatic in32%pts. Results regarding histology and treatments will be presented as well.

Conclusions: These are preliminary results from the largest prospective NEN registries in Greece. Due to the increased training of NEN specialists in pathologyand the improved imaging methods, NENs are increasingly recognized. However, a large percentage of pts arediagnosed in locally advanced or metastatic stages. It is necessaryto improve the rates of early diagnosis and identification of NENs.

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HIGH FREQUENCY OF PATHOGENIC VARIANTS IN EPITHELIAL OVARIAN CANCER PATIENTS – COMBINATION OF GERMLINE AND TUMOR GENETIC TESTING OFFERS THE OPTIMUM DIAGNOSTIC BENEFIT

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Epithelial Ovarian Cancer (EOC) diagnosis can be used as a standalone criterion for genetic testing referral, regardless of family history or age at diagnosis. The purpose of the present study is the identification of pathogenic variants in genes, the protein products of which participate in DNA repair through homologous recombination, in EOC patients. Through the discovery of such variants, appropriate candidates for targeted therapy with PARP inhibitors can be identified.

Germline DNA from 944 EOC patients was collected and analyzed for the presence of pathogenic variants in 94 genes implicated in DNA repair and/or cancer predisposition, through the utilization of Trusight® Cancer Panel. Additionally, 111 tumors were collected, from patients with a negative germline test result and analyzed for the presence of somatic pathogenic variants in the *BRCA1* and *BRCA2* genes.

In total, 34% (321/944) of patients carried germline pathogenic variants in 13 genes known to be associated to EOC predisposition. Apart from *BRCA1 & BRCA2* pathogenic variants, which represented 88.4% of the total findings, *RAD51C* pathogenic variants were the next most common identified, representing 4,1% of the findings. The vast majority of germline genetic defects (97.1%) were observed in genes participating in the homologous recombination repair pathway. Subsequently, 11,7% (13/111) of ovarian tumors bore somatic *BRCA1 & BRCA2* pathogenic variants, with variant allele frequencies (VAF) ranging from 9% to 47%.

The present work highlights the remarkably high frequency of pathogenic variants in HR genes, discovered through sequential screening of germline and tumor DNA of EOC patients. This is a significant contribution to the proper identification of suitable candidate patients for targeted therapies.

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CELL-FREE CIRCULATING DNA KINETICS AND DNA METHYLATION MARKERS AS PROGNOSTIC FACTORS FOR SURVIVAL OF PROSTATE CANCER PATIENTS

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Introduction: Cell-free DNA levels are distinctly increased in most patients with prostate cancer (PCA). It is established that a small fraction of the DNA is derived from the tumor itself and epigenetic (DNA methylation) alterations are regularly detected in patients with PCA. The detection of increased DNA levels and tumor-specific DNA methylated sequences may provide diagnostic and prognostic information.

Aim: The aim of the present study was to analyze the cfDNA concentrations at different time points and to detect DNA methylation profile of *APC* and *RASSF1A* genes, in order to assess the value of these biomarkers for prognosis.

Methods: Plasma samples were obtained from 50 patients with metastatic prostate cancer, at the beginning of the first-line treatment (baseline), one month and two months later. Cell-free circulating DNA was isolated from 500 μL of plasma, using a commercially available kit and quantified using a fluorometer. Plasma from 25 healthy individuals was collected and used as a control group. The extracted DNAs were subjected to a sodium bisulfite conversion reaction. Real time methylation specific PCR for each gene was performed.

Results: The median levels of cfDNA in the baseline samples of PCA patients ($n = 50$) were higher than controls ($n=25$) but tend to diminish during the different time points. At the baseline *APC* was found to be methylated at 29/50 (58%) and *RASSF1A* 32/50 (64%), but no significant alteration at the methylation levels of these two genes was observed at the following time points. In the survival analysis, the group with baseline methylated *APC* and *RASSF1A* tend to not reach the median survival point. Furthermore, there were strong positive correlations between Gleeson score *APC* and *RASSF1A* methylation (P values <0.04).

Conclusions: These results are promising and further studies in a larger cohort of patients are required to explore the prognostic significance of these markers in metastatic prostate cancer.

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ADVANCED LUNG CANCER INFLAMMATION INDEX (ALI SCORE) AS A BIOMARKER OF IMMUNOTHERAPY EFFICACY IN PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER

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Introduction To date, there is no optimal surrogate of immunotherapy efficacy in advanced non-small-cell lung cancer (NSCLC). Advanced Lung Cancer Inflammation Index (ALI score: body mass index X serum albumine/blood neutrophil-to-lymphocyte ratio) reflects the systemic inflammation of the host and is easily reproducible in routine clinical practice.

Methods We retrospectively analyzed patients with stage III or IV NSCLC who received PD1/PD-L1 inhibitors alone or in combination with chemotherapy in any line of treatment in 25 cancer centers in Greece. For every patient we recorded demographic, somatometric and clinicopathological characteristics, as well as clinical outcomes of immunotherapy. ALI score was evaluated as a marker of efficacy through appropriate statistical tests.

Results Seven hundred and three (703) patients were included in final analysis, of whom 71.7% were men, 67.2% had tumors of adenocarcinoma histology, 88.4% had stage IV disease at diagnosis, 39.4% received immunotherapy as 1st-line treatment and 74.9% as monotherapy. Median age at diagnosis was 68 years, median BMI was 25.1 kg/m2, median albumin level was 3.9 g/dl and 35.4% of the patients had PD-L1 expression>50%. Using the bibliographic cut-off value of 18 for ALI, patients with ALI>18 had significantly longer PFS (12 vs 5.6 months, $p<0.001$) and OS (23.1 vs 12.0 months, $p<0.001$). In multivariate analysis, patients with ALI>18 had a 42% lower probability of disease progression and 50% lower probability of death as compared to those with ALI<18, independent of Performance Status, stage at diagnosis, line of treatment and level of PD-L1 expression. There was no statistically significant correlation of ALI with objective response rates to immunotherapy (PD vs CR or PR or SD, $p=0.623$).

Conclusions ALI score correlates with clinical benefit from immunotherapy in advanced NSCLC and may assist decision-making in clinical practice.

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APPROPRIATE TREATMENT SELECTION IN HARD TO TREAT CANCERS USING NGS: DETERMINATION OF A COMPREHENSIVE TUMOR PROFILE

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Introduction: The analysis of the molecular profile of tumors is now becoming a reality, mainly due to next-generation sequencing technology (NGS) and can be used to personalize the therapeutic approach in cancer patients.

Aim: The present study aimed to investigate the molecular profile results obtained by using a pancancer NGS panel for cancer treatment selection. A variety of tumor types have been analyzed, including aggressive and hard to treat cancers such as pancreatic cancer. Besides, the clinical utility of immunotherapy biomarkers (TMB, MSI, PD-L1) was also explored.

Methods: NGS analysis was conducted using a panel of 161 genes in tumor tissues from 451 cancer patients. Furthermore, analysis of Microsatellite Instability, Tumor mutational burden (TMB) and PD-L1 expression analysis was performed in 201 cases.

Results: 451 patients with various types of cancer were analyzed, such as pancreas, lung, breast, colon, ovary, prostate, brain, and others. A total of 594 pathogenic mutations in 91 genes were detected in 76.5% of the patients analyzed. 7.10% of the patients harbored a mutation in a gene of homologous recombination, which could be used as a predictive biomarker of response to treatment with PARP inhibitors. 33.37% of patients had a mutation in a gene associated with on label or off label treatment, while 42.13% of the findings could give them access to a clinical trial. Regarding immunotherapy markers, microsatellite instability was detected in 3.89% and PD-L1 positivity in 30.49% of patients. TMB showed a significant variation between patients, with a minimum value of 1.9 and a maximum of 82.8 mutations/MB. In addition, as expected, the median TMB value varied among cancers with the lowest value being observed in sarcomas and the highest in NSCLC.

Conclusions: The multigene NGS analysis allowed the simultaneous analysis of predictive biomarkers in both targeted therapies and immunotherapy, identifying a clinically important finding in 75.5% of patients tested.

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METASTATIC EXTRAMAMMARY PAGET'S DISEASE : CASE REPORT

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Introduction: Extramammary Paget's disease (EMPD) is a rare intraepithelial carcinoma and accounts for only 6.5% of Paget's disease. It appears as an erythematous plaque and it is usually associated with carcinoma of the apocrine sweat glands (primary) or colorectal and urogenital cancer (secondary). Although it usually develops slowly, in 20% of cases it can progress into invasive carcinoma and give lymph node and distant metastases. To date, various chemotherapeutic regimens have been tested in metastatic EMPD, as well as drug combinations including trastuzumab in HER2 (+) tumors, but the prognosis generally remains poor, with a median survival of approximately 1.5 years.

Aim: The description of a rare case of metastatic EMPD and the review of bibliographic data concerning the therapeutic approach.

Case: A 67-year-old woman was diagnosed with non-invasive perineal Paget's disease 10 years ago. Due to local recurrence, she underwent vaginectomy 4 years ago and since then follow-up biopsies were performed every 6 months because of positive surgical margins. 1.5 years ago, she developed swelling and redness of the lower left extremity related to lymphedema. Diagnostic imaging showed a solitary liver metastasis and pathologically enlarged inguinal, iliac and paraaortic lymph nodes. An inguinal lymph node biopsy revealed a poorly differentiated adenocarcinoma CK7 and CK20 positive, CDX2, PAX8, uropladin, TTF1, P63, HER2 negative, consistent with the known Paget's disease. Further staging with mammography, breast MRI, cystoscopy and colonoscopy did not reveal any pathological findings. Eventually the patient began chemotherapy with docetaxel and carboplatin based on data showing docetaxel activity as monotherapy or in combination with S-1. Serial imaging tests after 8 cycles of treatment showed an ongoing response with reduction in the size of the liver lesion, disappearance of the enlarged lymph nodes and improvement of the lymphedema. Since the last 3 months the patient has been taking a treatment break and she remains in good clinical condition.

Conclusion: Metastatic EMPD is a carcinoma with a poor prognosis and very few data exist on its treatment. The case of our patient shows that the combination of docetaxel/carboplatin could be added to the therapeutic quiver for this rare disease.

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OBSERVATIONAL STUDY OF THE CLINICAL PRACTICE IN PATIENTS WITH RESECTABLE OR BORDERLINE RESECTABLE OR ADVANCED PANCREATIC ADENOCARCINOMA IN GREECE

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Introduction: The purpose of this prospective multicenter observational study was to describe the clinicopathological and treatment characteristics of patients (pts) with pancreatic adenocarcinoma (PC) in Greece. Secondarily, the study aimed to collect data about the effectiveness of the local and systemic therapies in terms of survival parameters.

Methods: Clinicopathological and treatment data were prospectively collected from 2/2016 to 2/2018 from the files of 200 pts in 20 participating centers. Disease-free survival (DFS), progression-free survival (PFS) and overall survival (OS) were analyzed by the Kaplan-Meier method.

Results: Median age at PC diagnosis was 65 years (range 17-84) and male-to-female ratio was 1.2.Median body mass index was 23.8 (range 14.2-37.8). PS(ECOG) was 0 in 88 (44%) pts. Baseline median serum CA19-9 levels were370 U/mL (range 0.6-1,000,000). Rare histological subtypes were acinar cell carcinoma in 3 (1.5%) pts, adenosquamous carcinoma in 3 (1.5%), squamous cell carcinoma in 1 (0.5%) and mucinous carcinoma in 1 (0.5%). Seven pts (3.5%) were diagnosed with stage I, 11 (5.5%) with stage IIA and 35 (17.5%) with stage IIB. Of them, 41 (77.4%) pts received adjuvant and 2 (3.8%) neoadjuvant chemotherapy. Median DFS was 24.9 months (95%CI, 16.9-33.0) and median OS 40 months (95%CI, 25.3-54.6). Also, 24 pts (12%) were initially diagnosed with stage III and 119 (59.5%) with stage IV. Eighty pts with stage IV disease had liver (67.2%), 22 had distant lymph node (18.5%) and 18 had peritoneal metastases/ascites (15.1%), while 49 (41.2%) had metastases in other organs.Of pts with stage III/IV disease, 88 (61.5%) received nab-paclitaxel/gemcitabine, 24 (16.7%) received FOLFIRINOX/XELOXIRI, 16 (11.2%) gemcitabine monotherapy and 13 (9.1%) other regimens. Median PFS was 7.8 months (95%CI 6.5-9.2) for stage III and 7.1 months (95%CI 5.2 – 9.0) for stage IV pts. Median OS was 14.2 months (95%CI 9.2 – 19.2) for stage III and 13.5 months(95%CI 11.5 – 15.4) for stage IV pts.

Conclusions: In this study, we described the status of care of pancreatic cancer in Greece in an attempt to improve the therapeutic standards.

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PREVALENCE OF SARCOPENIA ACCORDING TO INTERNATIONAL DIAGNOSIS CRITERIA IN ONCOLOGY PATIENTS PRIOR TO TREATMENT INITIATION. ASSOCIATIONS WITH OVERALL SURVIVAL.

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Introduction: In 2019, European Working Group on Sarcopenia in Older People (EWGSOP2) revised the consensus criteria on definition and diagnosis for sarcopenia.

Aim: To estimate the prevalence of sarcopenia by applying the recently revised definition criteria in a sample of newly diagnosed elderly patients with metastatic tumors prior to treatment initiation.

Methods: Patients >65 years old, referred for induction/first line therapy were eligible. Handgrip Strength (HGS) was used to estimate muscle strength and skeletal muscle index (SMI) from computed tomography in the 3rd lumbar vertebra (L3) was used to estimate muscle mass (muscle quantity). Gait Speed Test (GST) was used to assess physical performance status for the assessment of sarcopenia severity.

Results: In total 45 patients (69% men) with mean age [± Standard Deviation (SD)] 77.4 years (± 6.8 years) were evaluated. 42.2% of the patients (n=19) were classified as sarcopenic. Sarcopenia severity was estimated for 34 patients for whom gait speed test was available, with 23,5% of the sample (n=8) being severe sarcopenic. Patients mean values (±SD) for HGS, SMI and GST was 25,6 kg (± 9.3), 42,9 cm^2/m^2 (± 6.9) and 0.87 m/sec (± 0.3) respectively. From the confounding factors that were analyzed, older age significantly affected the prevalence of sarcopenia (p value =0.002). Survival analysis showed that non-sarcopenic patients achieved a significantly higher overall survival compared with sarcopenic patients (12.9 months vs 6.0 months), p = 0.02. Based on multivariate cox regression analysis presence of sarcopenia increased the risk of death by 68% after adjustment for age and tumor site (HR 0.32 95% CI 0.12-0.87, p = 0.02).

Conclusions: Prevalence of sarcopenia, using the international consensus definition criteria according to EWGSOP2, is high in elderly patients with metastatic cancer already at the time of the diagnosis. Presence of sarcopenia is independently associated with shorter overall survival.

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ACT FOR PREVENTION AND PROPHYLAXIS OF CANCER ASSOCIATED THROMBOSIS (CAT)

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Introduction: CAT is the 2nd leading cause of death in oncology patients and there is need for thrombosis management across the natural history of cancer because of its dynamic nature. Anticoagulant therapy is the cornerstone of prevention and treatment, since thrombosis interferes with cancer treatment, increases health care resource utilization, imposes emotional and economic burden.

Methods: A prospective observational study conducted by HeSMOacross Greece, aiming to record the clinical practice of CAT prophylaxis in patients with solid tumors. Ambulatory, high risk for thrombosis,activecancer patients who received thromboprophylaxis are enrolled after signing informed consent.

Results: Preliminaryresultsare collected from 17 oncology departments. From the 272 enrolled patients, 176 (64.7%) have completed second visit (3-4 cycles of anticancer treatment). Primary cancers included: lung 31.3%, pancreas 26.1%, colorectal 13.6%, gynecological cancers 10.2%, stomach 7.8%, bladder 6.3%, and others. 75.6% of the patients had metastatic disease. 1/3 of the patients were smokers or ex-smokersand 33% underwent surgery. Most ofpatients (65.9%) were at 1st line treatment and 17.6% at 2nd line.The vast majority (90.3%) were treated with High-Risk for Thrombosis Chemotherapy Agents (HRTCAs) such as cisplatin etc. Regarding Khorana score, 65.1% of patients had ≥2. In particular, 86.7% of patients with Khorana score ≤1 received HRTCAs while 95.4% of patients with score=2.All patients received thromboprophylaxis, specifically: 93.0% tinzaparin, 5.2% fondaparinux and 1.8% other (enoxaparin, bemiparin) with average duration 5.3±3.1 months. 67.1% of patients received higher than standard prophylactic doses.3 patients (1.7%) experienced thrombotic events (2DVT and 1 PE). These 3 patients had metastases and were treated withHRTCAs. Fivegrade 1 bleeding events were reported (2.8%).

Conclusions: Thromboprophylaxis of CAT is both safe and effective. Oncologists are alerted about CAT negative influences in cancer patients' prognosis. Apart from Khorana score, factors such as metastases, use of HRTCAs along with drug-drug interactions, increase the LMWHs usage often in higher than prophylactic doses in CAT management.

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PROGNOSTIC ROLE OF INFIAMMATORY BIOMARKERS IN PATIENTS WITH ADVANCED PANCREATIC ADENOCARCINOMA UNDERGOING FIRST-LINE CHEMOTHERAPY

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Introduction: The aim of the current study was to examine the prognostic significance of inflammatory biomarkers in patients with locally advanced or metastatic pancreatic adenocarcinoma undergoing first-line chemotherapy with nab-paclitaxel and gemcitabine.

Aim: To investigate the prognostic role of infiammatory biomarkers in patients with advanced pancreatic adenocarcinoma undergoing first-line chemotherapy.

Methods: In the current cohort study data from 57 patients were retrospectively collected. All patients had histologically or cytologically confirmed pancreatic locally advanced or metastatic adenocarcinoma and were treated with first-line nab-paclitaxel and gemcitabine from July 2014 to February 2020. White cell (WBC), neutrophil (NEUT), lymphocyte (LYMPH), monocyte (MONO) and platelet (PLT) blood levels during the last two days before the start of the first cycle of chemotherapy were measured. Median neutrophil to lymphocyte ratio (NLR), median monocyte to lymphocyte ratio (MLR), median systemic inflammatory response index (SIRI=NEUT × MONO/LYMPH) and median platelet-to-lymphocyte ratio PLR were calculated.

Results: Median age was 67 years (range, 43-81), while 29 (50.9%) male and 28 (49.1%) female patients were included in the study. PS (ECOG) was zero in 32 (56.2%) patients, one in 21 (36.8%) and two in 4 (7.0%) patients. Forty seven (82.5%) patients had stage IV and 10 (17.5%) had stage III disease. After a median follow-up of 20.6 months (range, 1.1-37.3), 48 (84.2%) developed progressive disease and 41 (71.9%) died of disease. Median progression-free survival (PFS) was 5.1 months (95%CI, 3.6-6.6) and median overall survival (OS) was 9.9 months (95%CI, 6.2-13.6). Patients with stage III had median PFS 9.2 months (95%CI 3.0-15.4), while stage IV patients had median PFS 5.1 months (95%CI 3.3-6.9), with statistically significant difference (p=0.011). Increasing NLR levels were correlated with poorer PFS (HR 1.10, 95%CI 1.01-1.20,p=0.033) but not with OS (HR 1.07,95%CI 0.98-1.18,p=0.139). Cox proportional hazard models confirmed that higher NLR levels were independently associated with poorer PFS (HR 1.14, 95%CI 1.03-1.25, p=0.009) and poorer OS (HR 1.11, 95%CI 1.01-1.23,p=0.037). Also, PS ECOG 1-2 (compared to PS 0) showed independent prognostic significance for PFS (HR 2.51, 95%CI 1.34-4.69,p=0.004) and OS (HR 3.00, 95%CI 1.53-5.76, p=0.001). In contrast, tumor stage did not demonstrate independent prognostic significance. Exploratory analysis examined the prognostic significance of different NLR cutoffs (by increasing the NLR value by 0.5) for PFS and OS. The best cutoff was NLR ≥4 vs. <4. Median PFS of patients with NLR ≥4 was significantly shorter compared to NLR <4 (3.1 vs. 6.0, respectively, p=0.005). Also, median OS of patients with NLR ≥4 was significantly shorter compared to NLR <4 (5.7 vs. 11.5, respectively, p=0.025). Subgroup analysis showed that patients with PS ECOG 0 and NLR <4 had the longest median PFS compared to the group with PS ECOG 1-2 or NLR ≥4 and the group with PS ECOG 1-2 and NLR ≥4 (7.1 vs. 5.1 vs. 2.0, respectively, p<0.001) and longest median OS compared to the group with PS ECOG 1-2 and NLR ≥4 (14.0 vs. 8.2 vs. 5.7, respectively, p<0.001).

Conclusions: The present retrospective analysis revealed clinically meaningful subgroups with distinct prognoses according to inflammatory biomarkers and performance status, irrespective of tumor stage, in patients with advanced pancreatic adenocarcinoma treated with first-line nab-paclitaxel – gemcitabine.

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CASE PRESENTATION: A RARE METASTATIC CUTANEOUS SQUAMOUS CELL CARCINOMA – THE USE OF CEMIPLIMAB IN CLINICAL PRACTICE

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Introduction: Cutaneous squamous cell carcinomas (SCC) with distant metastases are rare, yet more common than metastatic basal cell carcinomas. The average risk of distant metastatic disease is only 0,4%, risk of lymph node metastasis is 3,7%, and risk of disease-specific death is 2,1%. There is no standard treatment, and unfortunately, evidence regarding systemic therapy is limited.

Aim and methods: We aim to present a patient with metastatic SCSC that was treated with cemiplimab, a new monoclonal antibody that targets checkpoint inhibitor PD-1.

Results/Case presentation: A 59-year-old female patient was diagnosed in December 2018 with SCSC of the right sole, on a site-specific sunburn during childhood. PET-CT revealed enlarged inguinal lymph nodes but no other sign of distant metastasis. The patient underwent wide local excision of the primary tumour and regional lymph node dissection. The pathology revealed a T3N2bG1-high risk SCC (40mm in max diameter, high mitotic rate, Breslow 12 mm, Clark IV, R0, ulceration and 2/11 lymph nodes were positive < 3cm). She was treated with 50Gy of adjuvant radiotherapy (25fr x 2Gy). One month later, the CT scans showed multiple pulmonary metastases, and she received first-line platinum-based treatment (carboplatin/5FU/paclitaxel). The best response was stable disease, which lasted four months. Subsequently, she presented with local recurrence on her right calf, on a previously irradiated area. The new lesion was excised with clear margins (SCSC 17mm, gr.II, Breslow 5,9mm, Clark IV, high mitotic rate). Due to concurrent disease progression in lung metastases, we started second-line treatment with cemiplimab 350mg q21d. After three cycles, the patient was hospitalized with pneumonitis gr.III that required oxygen supply and steroids intravenously. After recovery, we restarted cemiplimab at the initial dose, and recent imaging revealed partial response to treatment (PR).

Conclusions: Metastatic SCSC are rare conditions, and evidence from prospective phase III studies regarding systemic therapy is limited. This case is in concordance with early phase clinical trials showed that treatment with cemiplimab is feasible with potentially positive results.

References: Michael R.Migden et al, PD-1 blockade with Cemiplimab in Advanced Cutaneous Squamous Cell Cancer, NEJM, 26 July 2018

Abbreviations: SCSC: squamous cell skin cancer, PD-1: programmed death 1, PR: partial response

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CONTRIBUTION OF SAMARIUM 153Sm EDTMP TO THE ALTERATION OF BONES METABOLISM MARKERS AT SYMPTOMATIC BONE METASTASES, BEYOND ITS ANALGESIC EFFECT.

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Study in progress under sponsorship granted from the Hellenic Society of Medical Oncology (HeSMO)

Introduction: Samarium-153 is a radionuclide that is selectively bone bound to the skeleton and especially in areas with intense osteoblastic activity. The result is effective relief of bone pain in patients with multiple painful osteoblastic skeletal metastases. Intermediate response to pain is reported in 80% of patients with breast cancer and 56-74% with prostate cancer.

Aim: The investigation of possible antineoplastic activity of ^{153}Sm EDTMP in bone metastases.

Methods: Patients with painful bone metastatic disease for at least 3 months, without having received bone targeted therapy or radiotherapy. Analgesic treatment concerned standard analgesic regimens and / or NSAIDs. Thereafter, values shall be recorded before and after each application of the ^{153}Sm EDTMP (1mCi/kg) of the following osteoblastic markers, P1CP collagen type I carboxyellate propeptide and P1NP aminofinal collagen type I propeptide. Measurements shall be performed by the ELISA method. To date, seven patients aged 40 to 80 years, ECOG performance status 0-1 with multiple painful bone metastases, have been introduced in the study. Three from Prostate cancer and four from breast cancer.

Results: A comparison of markers of bone metabolism and osteoblastic activity, before and after administration of 153Sm EDTMP, shows in the majority of cases a significant increase in markers indicating repair of bone damage through increased osteoblastic activity.

Conclusions: Despite the small number of patients in this ongoing study, the results suggest an effect of ^{153}Sm EDTMP on osteoblasts as well as on cancer cells.

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DETECTION OF MICROBIAL DNA IN THE BLOOD OF COLORECTAL CANCER PATIENTS FOR THE DIAGNOSIS OF MICROBIAL TRANSLOCATION

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Background:	Dysbiosis has been associated with diseases and is of a major public health importance. Can lead to the passage of viable bacteria, their products or their fragments from the intestinal lumen through the mesenteric lymph nodes and other sites, known as bacterial translocation.
Aim:	To determine if microbial translocation occurs in stage II/III-IV colorectal cancer (CRC) patients and evaluate the usefulness of blood PCR for diagnosis of such translocation. Also to correlate the presence of Toll-Like Receptor and Vitamin D Receptor polymorphisms with the detection of microbial DNA fragments in the blood of CRC patients.
Materials and Methods:	Peripheral blood was obtained from 397 CRC patients (adjuvant n=202 and metastatic n=195) and 32 healthy indviduals. DNA from all subjects was analyzed using PCR for amplification of genomic DNA encoding 16S rRNA, β-galactosidase gene of *E. coli*, Glutamine synthase gene of *B. fragilis* and *5*.8S rRNA found in *C. albicans*.
Results:	Significantly higher rates of 16S rRNA, β-galactosidase, Glutamine synthase and *5*.8S rRNA detection was observed in the pool of CRC patients than the controls ($p<0.001$). All microbial DNA fragments detected were also significantly associated with the metastatic disease ($p<0.001$) leading to shorter survival rates ($p<0.001$). Moreover, individuals with the homozygous mutant alleles of either TLR or VDR gene polymorphisms had significantly higher detection rates of microbial DNA fragments.
Conclusions:	The detection of microbial DNA fragments in patients with CRC highlights the role of these microbes in cancer development, progression and therefore in patients' survival.

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CLINICAL AND DOSIMETRIC PROGNOSTIC FACTORS OF LATE RECTAL BLEEDING AFTER RADICAL RADIATION THERAPY FOR PROSTATE CANCER

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Introduction: Late rectal bleeding has a negative impact to the quality of life of patients with prostate cancer who have received 3D conformal radiation therapy treatment(3D-CRT).

Aim: Our aim was to investigate the incidence of rectal bleeding due to radiation therapy for prostate cancer and to correlate rectal bleeding with dosimetric and other factors as treatment with anticoagulants agents.

Methods: Sixty-four patients with intermediate and high risk prostate cancer were investigated retrospectively. All received 3D-CRT to a total dose of 7000 cGy in 35 daily fractions. Most of the patients (81.7%) received neoadjuvant and concurrent hormone therapy. Late rectal bleeding toxicity was defined according to EORTC criteria for adverse events (Common Terminology Criteria for Adverse Events v4.0).Clinical factors investigated were the administration of anticoagulants agents and hormone therapy. Dosimetric factors taken into consideration were the V50 and V60 of rectum.

Results: Median time for the appearance of rectal bleeding was 17.4 months with range 9-49 months. From 64 patients ,16 suffered from Grade 1 bleeding which was treated with local administration of sterinoids. Ten patients presented Grade 2 bleeding and only one patient had serious bleeding of Grade 3. All were treated with argon plasma laser coagulation therapy (APC). Eight patients(61,5%) from the eleven with Grade 2 and 3 bleeding had also a second session of APC. None of the patients developed important bleeding after the second session. Four patients that developed grade 2 toxicity were under treatment with anticoagulants agents. During the retrospective analysis of dose volume histograms(DVH)we discovered important differences to the mean value of V60 and V10 between toxicities grades of 0-1 and 2-3.To the 13 patients with rectal bleeding of grade 2 and 3 V50 was between 45-50% and V60 was >35%.

Conclusions: Our results are consistent with international publications and indicate the possible association of grade 2 or 3 rectal bleeding with the intake of anticoagulants agents and radiation dose that rectum receives during treatment(V50-V60.).Hormone therapy was not associated with late toxicity as rectal bleeding.

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PNEUMONITIS ASSOCIATED WITH PACLITAXEL IFOSFAMIDE AND CISPLATIN CHEMOTHERAPY IN A PATIENT WITH LOCALLY ADVANCED PENILE CANCER

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Introduction: Paclitaxel induced interstitial pneumonitis is a well-defined hypersensitivity reaction that has been mostly described in cancers of breast and lung. A great percentage of these cases are associated with either concurrent or previous irradiation of the chest, with the latter known as radiation recall pneumonitis.

Aim: We present the case of a middle-aged, chemotherapy- and radiotherapy- naïve patient with locally advanced penile cancer, who developed severe pneumonitis shortly during the first course of paclitaxel, ifosfamide and cisplatin administration. We emphasize on the particular "crazy – paving" appearance of pneumonitis on chest CT and the rapid clinical and imaging improvement with high dose steroids.

Case: A 50 year–old male with a recent diagnosis of locally advanced penile squamous cell carcinoma was referred to our department as a candidate for neoadjuvant chemotherapy. After the appropriate premedication dose of dexamethasone, the patient was started on chemotherapy by receiving paclitaxel 175 mg/m^2 on day 1, ifosfamide 1200 mg/m^2 and cisplatin 20 mg/m^2 from day 1 to day 3. However, during the 2nd day of treatment the patient presented acute dyspnea and nonproductive cough, leading to treatment discontinuation. The symptoms along with hypoxemia were suggestive of rapidly worsening respiratory function, while physical examination revealed bilateral fine crackles. Urgent computed tomography of the chest uncovered a combination of ground glass opacity with superimposed septal thickening, mainly in the upper fields of both lungs. The appearance of these findings is characteristically described under the term "crazy – paving pattern" and accounts for a less common imaging manifestation of drug–induced pneumonitis. Based on other reports and the temporal relationship of onset of symptoms (approximately 24 hours after paclitaxel infusion) paclitaxel was considered as the most likely culprit for interstitial pneumonitis. Prompt administration of high dose corticosteroids (methylprednisolone 2 mg/kg) resulted in quick significant recovery. Indeed, clinical improvement was reflected to the comparative CT scan, 5 days later, that showed remarkable radiological improvement with complete resolution of lesions.

Conclusions: To our knowledge, this is the first report of interstitial pneumonitis attributable to TIP chemotherapy regimen. Clinicians should be aware of the potentially life-threatening pulmonary toxicity following this regimen. Early administration of high-dose steroids seems critical in the successful management of this emergency situation.

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CASE REPORTS OF UROTHELIAL CARCINOMA WITH SOLITARY BONE METASTASIS

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Introduction: Bladder cancer consists the commonest malignancy involving the urinary system with urothelial carcinoma to be the predominant histologic type. It is recorded as the second most common urinary tract malignancy in men and is responsible for more than 80,000 new cases and almost 18,000 deaths yearly. 10-15% of patients appear to have metastatic disease during diagnosis. Bone metastases are not frequent and usually follow other systemic metastases.

Case reports: The first patient is a 56-year-old male that underwent radical cystectomy. The histological examination revealed a pT4aN0 low differentiated urothelial carcinoma and adjuvant chemotherapy with cisplatin/gemcitabine was administered. Four years later, an histologically confirmed solitary bone metastasis in left ankle was found. The patient received radiotherapy and remained progression free for 3 years before the appearance of new bone metastases in the middle of left tibia and lumbar vertebrae. The second patient is a 58-year-old male with an histological examination obtained after radical cystectomy representing a low differentiated pT3bN0 urothelial carcinoma. According to the new imaging examination performed a month after cystectomy because of continuous left tibia pain, a lytic bone lesion in the middle of the left tibia was discovered and therefore the patient underwent preventive static intramedullary nailing of tibia. The biopsy of this lesion revealed metastatic invasion of bladder cancer while the rest imaging testing remained negative. 1st line chemotherapy with cisplatin/gemcitabine was administered in combination with lesion radiotherapy with a progression free interval of six months.

Discussion: According to recent studies, the incidence of bone metastases in patients with bladder cancer is about 5,5%. Nevertheless, it is not clear if searching bone metastases in asymptomatic patients consists a cost effective approach.

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CLINICAL SIGNIFICANCE OF TRANSCRIBED ULTRACONSERVED REGIONS (T-UCRS) UC160, UC283 AND UC346 IN COLORECTAL CANCER

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Introduction: Transcribed Ultra-Conserved Regions (T-UCRs) Uc160, Uc283 and Uc346 have been shown that undergo CpG island methylation in their promoter regions, which results in their transcriptional silencing in colorectal cancer (CRC), while they are transcribed in the adjacent non-malignant tissues.

Aim: The present study explores the possible alterations in methylation levels of Uc160, Uc283 and Uc346 during CRC development and progression and their clinical significance for CRC patients' survival.

Methods: Promoter methylation of Uc160, Uc283 and Uc346 was detected using methylation-on-beads and real-time quantitative Methylation Specific PCR (qMSP) in 137 CRC and 49 adenoma tissues, as well as in 35 infiltrated lymph nodes and 11 liver and lung metastatic lesions. Their transcription was assessed in representative sample tissues using in situ hybridization. Moreover, T-UCRs mRNA levels were assessed in the colon cancer cell line HT-29 before and after resistance to chemotherapeutics 5-fluorouracil (5-FU) and oxaliplatin.

Results: A gradual increase in methylation levels was observed from hyperplastic polyps to adenomas and in situ carcinomas, while a gradual decrease was observed in infiltrating and metastatic carcinomas ($p<0.001$ for Uc160 and Uc283, $p=0.018$ for Uc346). Moreover, methylation levels of Uc160 and Uc283 were positively associated with grade of dysplasia ($p=0.034$ and $p=0.019$, respectively). Higher methylation levels of Uc160 were associated with longer overall survival of advanced stage CRC patients, in univariate ($p=0.009$, HR=0.366) and multivariate analysis ($p=0.005$, HR=0.240). Similarly, higher methylation levels of Uc283 were associated with longer overall survival ($p=0.030$) and disease-free survival ($p=0.038$). Finally, mRNA levels were significantly lower in colon cancer cells resistant to oxaliplatin ($p<0.001$ for all three T-UCRs).

Conclusions: The present study suggests that methylation levels of T-UCRs Uc160, Uc283 and Uc346 differ during CRC development and progression and Uc160 and Uc283 methylation is prognostic for CRC.

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ALVEOLAR RHABDOMYOSARCOMA WITH UNUSUAL CYTOGENETIC FINDINGS: A CASE REPORT PRESENTATION

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Introduction: Rhabdomyosarcoma (RMS) is a rare neoplasm, however the most common pediatric soft tissue sarcoma. The histological subtypes include the embryonal (ERMS), alveolar (ARMS), spindle-cell and pleomorphic rhabdomyosarcoma. ARMS has the worse overall prognosis and is characterized by specific cytogenetic alterations. These alterations display a recurrent translocation between genes encoding for transcription factor FKHR with either PAX3/PAX7. As a result, the chimeric genes encode transcription factors that promote tumorigenesis.

Aim: The presentation of a rare ARMS case report, which was diagnosed and studied with FISH analysis in our Hospital.

Methods: Histopathological examination, subsequent FISH analysis and literature review in PubMed/MEDLINE.

Results: A 12-year-old female patient, with no significant medical history, attended the emergency department, with dull inguinal pain symptoms. An abdomen CT scan revealed a 4cm pelvic mass. Since there were no metastases and the lesion did not infiltrate any regional structures, the patient was submitted to a local mass excision and pelvic lymph node dissection. Histologically are mentioned: R0 excision, absence of infiltrated lymph nodes and round, usually multinucleated tumor cells with mitotic figures. Paternless sheets of discohesive tumor cells with fibrovascular septae were also identified. Immunohistochemistry showed positivity for desmin, vimentin, myogenin and MyoD1. Therefore, the diagnosis of ARMS was suggested. FISH analysis for FKHR alterations, revealed one normal fusion signal, two split signals for the telomeric region of FKHR and multiple split signals for the centromeric region of FKHR. These results indicate gene translocation of FKHR3 region with simultaneous gene amplification and aneuploidy. The patient received postoperative adjuvant chemotherapy and radiotherapy. There was no recurrence at 6 months follow-up.

Conclusions: The uniqueness of the case is based on the simultaneously observed amplification, translocation and deletion of FKHR3 gene; a cytogenetic profile mentioned for the first time in the literature. In conclusion, FISH analysis contributes to the histological diagnosis of sarcomas. Additionally, the detection of unusual ARMS genetic subtypes is possible. The prominence of cytogenetic heterogeneity offers useful information for further histological classification of this rare tumor, with possible therapeutic and prognostic extensions.

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UNMET NEEDS OF PATIENTS WITH PANCREATIC CANCER IN GREECE: VIEWS OF HELTHCARE PROFESSIONALS

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Introduction: Pancreatic cancer is a disease with very high mortality and minimal therapeutic progress in last decades. It's the fourth leading cause of cancer death overall and the average life expectancy of patients does not exceed 1.5 years. There is very little research on the unmet needs of these patients in relation to other types of cancer.

Aim: Exploring the views of healthcare professionals about the providing care and their unsatisfied needs.

Methods: The study involved doctors and nurses of a cancer hospital. All participants had to work for at least one year in a clinic that carries patients with pancreatic cancer undergoing chemotherapy. The maximum variation was used as a sampling strategy. Eleven semi-structured interviews were conducted and recorded in mp3 format and then transcribed verbatim on MS Word. Qualitative thematic analysis was the selected method of analysis. The introduction of new participants into the study stopped when it reached the point of theoretical saturation and the interviews did not offer new concepts or contributed to the existence of the already recorded ones.

Results: Pain management is the main need of patients with pancreatic cancer undergoing chemotherapy. Psychological support is important for the majority of patients, even at the time of diagnosis. A number of non-physical symptoms are identified that are related to and affect the daily lives and quality of life of these patients. Dissatisfaction is expressed in the absence of palliative care structures and services. Finally, the participants addressed the need for an interdisciplinary approach to improve the quality of care of these patients.

Conclusions: In the present study, health professionals report a wide range of unsatisfied needs of patients with pancreatic cancer, with the majority expressing their concerns about the complete lack of patient support in the last stages of their lives.

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THREE-DIMENSIONAL CONFORMAL HDR BRACHYTHERAPY IN ENDOMETRIUM CANCER. CONTROL OF EFFECTIVITY AND STUDY OF TOXICITY. 3YEARS EXRERIENCE OF OUR DEPARTMENT.

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Introduction: Brachytherapy is an essential part of treatment in endometrium cancer.

Aim: The study of our experience during last three years in the management of endometrium cancer. It refers to the effectiveness and toxicity of this treatment approach.

Methods: From April 2018 to February 2020, 156 patients received 3D conformal HDR brachytherapy (range of age : 36-90 years). Only 2 patients were inoperable. Intravaginal cylinders were applied to operated patients and a wide variety of fractionation was followed. Patients who didn't receive adjuvant external beam radiotherapy, followed these fractionation schemes : 4 fractions x 7Gy/fr (31 patients) and 3 fractions x 7Gy/fr (41 patients). Patients who received adjuvant external beam radiotherapy, followed these fractionation schemes: 2 fractions x 7Gy/fr (38 patients), 3 fractions x 6 Gy/fr (19 patients), 2 fractions x 6 Gy/fr (18 patients). One patient didn't complete the brachytherapy protocol. Tandem of different curvature was applied to inoperable patients in conjunction to intravaginal cylinder. The curvature was decided based on the anatomical position of uterus. It is worth to refer that an intravaginal ultrasonography was very helpful to the estimation of uterus cavity length.

Results: Early toxicity of treatments was recorded. The most common side effects were related to mild enteritis (45%), especially when it was combined with EBRT, inflammation of vagina was quite common in the completion of treatment (30%), radiation cystitis with dysuria and frequent urination (most common to elderly patients). In terms of late toxicities, abnormalities to intestine habits (25%) and dyspareunia – dryness of vagina (35%) were recorded to patients younger than 50 years old. The most severe late effect was the sigmoid stenosis – early obstructive ileus in 2 patients (an operation was mandatory to one patient).

Conclusions: Three dimensional planning of brachytherapy treatment has minimized late side effects while early side effects are manageable and don't cause treatment interruption or extension of treatment time.

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DETECTION AND CLINICAL EVALUATION OF BRCA1 AND BRCA2 METHYLATION STATUS IN CELL-FREE DNA OF PATIENTS WITH EARLY GASTRIC CANCER

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Introduction: In recent years, the relationship between DNA methylation and cancer has been intensively studied. New biomarkers are emerging, which can be used to detect the primary tumor, recurrence, metastasis, and patient response to treatment. Aiming mainly at early disease, the detection of molecular markers of methylation, characteristics of malignant mutation and metastasis, may have been indicative of more intensive investigation or more regular follow-up.

Aim: The aim of the present study is to detect the methylation status of tumor suppressor genes BRCA1 and BRCA2 in the free-circulating DNA (cell-free DNA) of patients with early gastric cancer (n = 70). An additional objective of the study is to determine the concentration of cfDNA in plasma.

Methods: We used the real-time QUBIT fluorometer and real-time PCR (qReal Time PCR) specific for repeated ALU sequences, compared the above two methodologies and correlated the concentration of cfDNA with the clinical and pathological characteristics of patients.

Results: The BRCA1 and BRCA2 genes were found to be hypermethylated in the cfDNA of patients at 56.6% and 42.1%, respectively. A survival analysis showed that patients with non-methylated genes had a longer progression free survival (PFS) than those with methylated genes ($p < 0.009$ and $p = 0.013$, respectively). The overall survival (OS) was also higher for patients with non-methylated BRCA1 and BRCA2 genes ($p = 0.012$, and $p = 0.001$, respectively). Finally, it was shown that tumors located in the body of the stomach, showed a higher percentage of methylation of the BRCA2 gene, compared to tumors located in the antrum ($p = 0.006$).

Conclusions: Hypermethylation of tumor suppressor genes is an early event during carcinogenesis and remains during metastatic transformation. Methylation of the above genes appears to be a sufficient prognostic indicator of survival, however its value should be validated and confirmed in an even larger number of patients.

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A RARE CASE OF PLEURAL AND DIAPHRAGM METASTASIS IN SQUAMOUS CELL CARCINOMA OF PYRIFORM SINUS WITHOUT REGIONAL RECURRENCE

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Introduction: Head and neck cancer is the 6th most common cancer globally with numbers still rising in developing countries. Developments in treatment management have led to progression of free and overall survival. Metastatic disease usually appears in lungs, bones and liver following regional recurrence.

Case report: A 60-year-old male patient is diagnosed with stage IVa squamous cell carcinoma of left pyriform sinus and was treated with neoadjuvant chemotherapy with cisplatin, docetaxel and 5-fluorouracil followed by concomitant chemoradiotherapy. While being disease free, this patient was urgently hospitalized because of hypercalcemia and deteriorated respiratory function. There was no evidence of regional recurrence or metastatic disease according to the imaging tests, except for bilateral pleural effusions with the cytology obtained to be negative for malignancy. As the symptoms insisted, a new imaging scan was performed forty days later revealing a new intense bilateral nodular pleural thickness, tangential irregular swelling of diaphragm domes (mostly considering the left dome) and enlarged lymph nodes close to diaphragm. A pleural biopsy revealed moderately differentiated squamous cell carcinoma. Subsiquently, two cycles of chemotherapy with cisplatin, 5-fluorouracil and cetuximab were administered with poor outcome.

Discussion: Distal metastatic disease in squamous cell carcinoma of head and neck is rare, especially without evidence of local recurrence. More specifically, metastasis in pleura and diaphragm is considered extremely rare and referring to this case report, no other is reported in published literature till date.

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THREE-DIMENSIONAL CONFORMAL HDR BRACHYTHERAPY IN CERVIX CANCER. CONTROL OF EFFECTIVITY AND STUDY OF TOXICITY. 3YEARS EXRERIENCE OF OUR DEPARTMENT

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Introduction: Three dimensional conformal brachytherapy is a very important part of radical treatment in cervix cancer.

Aim: The recording and the study of our experience during last three years in the management of cervix cancer, refers to the control of effectiveness of this treatment approach and to the research of related toxicity.

Methods: During last three years, we offer treatment in 82 patients (range of age : 25-86 years). Twenty of them were operated. Sixty two patients had local advanced disease and were inoperable. The first group of patients received adjuvant brachytherapy with intravaginal cylinders following different fractionation schemes. Specifically, 7 patients received 3 fractions of 7 Gy each, 5 patients received 2 fractions of 6 Gy each. All the others follow different schemes. Only one patient with inoperable disease denied to receive all the fractions of brachytherapy. In inoperable patients, tandems of different curvature were used based on anatomical position of uterus. Before the application, an intravaginal ultrasonography took place estimating the length of uterus cavity. Most of the patients, 45 totally, with inoperable disease received 4 fractions of brachytherapy with 7 Gy per fraction.

Results: Early toxicity of treatments was recorded in detail. The most common side effects were related to mild enteritis (15%), inflammation of vagina that was presented at the end of the treatment (45%), radiation cystitis with dysuria and frequent urination (most common to elderly patients). As late effects, abnormalities to intestine habits (10%) and dyspareunia – dryness of vagina were recorded.

Conclusions: Our team prescribes weekly cisplatin concomitantly with external beam radiotherapy. We have the opportunity to plan the applications of brachytherapy in ideal intervals in relation to external beam radiotherapy. To summarize, following these rules, we manage to optimize the total treatment time for cervix cancer minimizing the toxicity at the same time.

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NEUROENDOCRINE NEOPLASM OF UNKNOWN PRIMARY ORIGIN AND BREAST CANCER

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Introduction: Neuroendocrine Neoplasms (NENs) are considered to be rare neoplasms. They are epithelial tumors with predominant neuroendocrine differentiation and can be developed in all types of tissues. Their histological, molecular and imaging characteristics aremostly indicative for their site of origin, but to a small extent it is difficult to find the primary site.

Case presentation: 83-year-old woman presented with a history of one yeardiarrhea, weakness, fatigue and anorexia. She also suffered from coronary disease, hypertension and hemorrhoids.Clinical examination revealed traces of blood in the digital anal examination as well as reduction of respiratory wheezing on the right lung. The laboratory testsshowed abnormal values for CEA, CA-125, NSEand chromogranin A.Imaging tests showed enlarged mediastinal and axillary lymph nodes as well as hepatomegaly, ascites and enlarged mesenteric and paraortic lymph nodes. Patient underwent colonoscopy that showed diverticulosis and rectal polyps with central ulceration and hemorrhagic lesion. The histology revealed a well differentiated, grade 3 (NETG3 WHO,2-4MF/10HPF, Ki67>20%), chromogranin(-), synaptophysin locally positive. She underwent gastroscopy that showed gastric polyps with central ulceration. The histology revealed infiltration of a well differentiated NET, grade 3 (NETG3 WHO,2-4MF/10HPF, Ki67>20% ~35-40%) chromogranin(-), synaptophysin locally positive. The octreoscan showed diffused bone marrow infiltration in the whole skeleton and visceral infiltration at the lower lobe of the right lung, liver and abdominal area. She underwent a bone marrow aspiration due to thrombocytopenia that showed diffused infiltration by epithelial origin malignancy, with strong positivity in oestrogen and progesterone receptors. A breast ultrasoundshowed a solid lesion at the left breast and histology of the lesion confirmed ductal carcinoma of the breast with positive hormone receptors and Her-2 negative. Review of all histologies tested revealed metastatic breast cancer. For this reason, patient received treatment with lanreotide 120mg and aromatase inhibitor with remarkable clinical improvement.

Conclusions: Neuroendocrine neoplasms usually present characteristics that lead us to the primary site, but sometimes it is difficult to conclude. These characteristics are not always indicative of the primary site as in our case in which diagnosis was achieved by bone marrow aspiration and has been confirmed by histology of the breast lesion.

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EVALUATION OF CHARACTERISTICS, RISK FACTORS AND THERAPEUTIC RESULTS OF CLOSTRIDIUM DIFFICILE INFECTION (CDI) IN ONCOLOGIC PATIENTS: A PERSPECTIVE STUDY

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Introduction: Clostridium Difficile Infection (CDI) has been increasing dramatically in the last decade. The most important risk factor in the general population patients is antibiotic use such as -lactam, quinolones and clindamycin. Literature data on CDI risk factors in oncologic patients are contradictory.

Aim: To investigate the prevalence, characteristics and possible risk factors of CDI in hospitalized oncologic patients.

Methods: Data of hospitalized patients in our department who were on or had discontinued their anti-neoplastic treatment and presented diarrhea from March 2018 to January 2020 were analyzed. Their medical history was studied and a stool sample was sent for CD toxin investigation.

Results: 79 oncologic patients (29 A, mean age 64 years, 35-87) were studied. 48.1% had a recent history of chemotherapy, 51.9% were on antibiotic therapy, 68.3% were using PPIs, 29.1% had a history of gastrointestinal surgery and 11.4% had undergone appendicectomy. A total of 10 patients (12.7%) presented CDI. Of these, 70% had a recent chemotherapy treatment, 60% were on antibiotic therapy, 60% were using PPIs, 30% had a history of gastrointestinal surgery, and 1 (10%) had undergone appendicectomy. The vast majority presented with an intermediate severity CDI (40%) while 1 (10%) patient presented with a severe infection. 1 (1.26%) patient died without his death being associated with the CDI. Statistical analysis of epidemiological and clinical parameters of patients who presented compared with those who did not present CDI showed a statistically significant relationship between CDI, PPIs use ($p = 0.040$) and the history of gastrointestinal surgery ($p = 0.016$).

Conclusions: In our study the prevalence of CDI is 12.7%. Statistically significant risk factors associated with CDI are the use of PPIs and a history of gastrointestinal surgery. Chemotherapy was not statistically associated with CDI.

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EVALUATION RESULTS FOR THE 25th HELLENIC CONGRESS OF CLINICAL ONCOLOGY (25th HCCO)

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[1]On behalf of the Hellenic Society of Medical Oncology - HeSMO (http://www.hesmo.gr/), Athens, Greece and the Organizing and Scientific Committee of the 25th HCCO

Introduction: The 25th HCCO "Unfolding the thread of Ariadne…for each of our patients" was organized by the Hellenic Society of Medical Oncology (HeSMO) in collaboration with the Hellenic Society of Radiation Oncology, the Hellenic Society of Surgical Oncology and the Hellenic Oncology Nursing Society and took place under the auspices of the European Society of Medical Oncology (ESMO). In particular, the 25th HCCO was held on April 18-20, 2019 in Athens and 560 delegates attended(315 oncologists, 85 doctors of other specialties, 68 nurses and 92 students) while 159 abstracts were submitted.

Method: All participants in the 25th ESCO were asked to complete an online evaluation form consisting of 23 questions (general, satisfaction, open).

Results: Received responses from 148 delegates with the following characteristics: men 59%, age: 36-45 40% and 46-55 30%, medical oncology 59%, radiationoncology 3%, surgical 1%, nursing 10% and other 22%, trainees 13% and specialists 70%, university hospital 26%, public 30%, private 17%, pharmaceutical company 9% and students 3%, Attica 58% and Thessaloniki 13%, members of HeSMO 53% and *HeGYO* 25%. Information for 25th HCCO: internet 51%, colleagues 35% and announcements 30%. Main reasons to attend 25th HCCO: participation as president-speaker-commentator-member of committees60%, scientific program 55% and review-update 47%. Participation at 25th HCCO: attendance 40%, speaker 28% and president 20%. Way of attendance: physical presence 90%, physical presence and live streaming 9% and live streaming only 1%. At what rate did you attend the 25th HCCO: 41-60% 39%, 21-40% 26% and 61-80% 20%. Participation in the opening ceremony 62%, closing ceremony 52%, HeSMO elections 48%, scientific event of HeGYO 32%, general meeting of HeSMO26% and scientific event of W4O 22%. The majority of delegates expressed overall satisfaction in various important dimensions. Indicatively, topics of conference (89%), duration of lectures (85%), interest of topics (90%), way of presenting the topics (85%), relativity of topics with work-specialty (91) %), expansion of scientific knowledge (85%), balance of program (89%), books of HeGYO / HeSMO (90%), awardfor best abstracts (82%), publication of abstracts in journal FCO of HeSMO(91%), pre-conference meeting (90%), conference website (88%), conference secretariat (95%), conferenceupdates (91%), conference space (95%) and exhibition space (89%). Finally, an important element of satisfaction is that the 82% of the delegates would attend the next HeSMO conference while 18% are unsure.

Conclusions: The annual conference of HeSMO is the biggest oncology conference in Greece and it is now well known, recognized and well attended by the Greek Oncology Community.

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EVALUATION OF PCI IN SCLC: SINGLE CENTRE EXPERIENCE

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Introduction: Small Cell Lung Cancer has worse prognosis in comparison with other types of lung cancer due to its biological characteristics. Prophylactic Cranial Irradiation, in those patients that is recommended, delays the occurrence of metastasis to the brain and increases overall survival.

Aim: The goal of this study is, through an experienced medical centre for the study and treatment of lung cancer, to review the role of Prophylactic Cranial Irradiation, in association with certain variables, in brain metastasis free survival and overall survival of patients with Small Cell Lung Cancer.

Methods: A review of 439 medical records of patients diagnosed with Small Cell Lung Cancer in Oncology Department of Sotiria General Hospital in Athens was performed. There were 66 patients among them who had undergone Prophylactic Cranial Irradiation (PCI). Statistical analysis of Overall Survival and Brain Metastasis Free Survival of these patients was done, in association with sex, age, performance status, method of diagnosis, plan of therapy, dose of irradiation, time since 1st chemotherapy and end of it till PCI.

Results: According to this study the possibility of Brain Metastasis Free Survival in patients with Small Cell Lung Cancer is 83% on 1st year, 54% 2-year survival and 48% 5-year survival. The possibility rate of Overall Survival for 1 year is 82% and 20% for 5-year survival. The only statistically significant variable for worse overall survival is poorer performance status after PCI.

Conclusions: Small Cell Lung Cancer patients have high probability to develop brain metastases affecting their quality of life and cause worse prognosis. Further research is needed, to effectively evaluate any possible association of Prophylactic Cranial Irradiation with other possible variables with aim to prolong overall survival.

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PATIENTS WITH SOLID TUMORS RECEIVING SYSTEMIC THERAPY REGARDING INFLUENZA AND PNEUMOCOCCAL IMMUNIZATION

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Introduction: Oncology patients represent an important population and a group with high sensitivity to infections. Solid tumors are a negative prognostic factor considering the infection incidence, hospitalization necessity and patients' mortality. Literature evidence proves that influenza and pneumococcal immunization is necessary for this population.

Aim: Recording the immunization of oncology patients and their compliance with updated guidelines for influenza and pneumococcal pneumonia prevention.

Methods: A prospective recording study of 380 patients with solid tumors under systemic therapy respectively with immunization towards influenza and pneumoniococcus and the appearance of related infection.

Results: Recorded patients were of median age of 64,1±11,9 years and were divided in 182 (47,9%) men and 198 (52,1%) women. Between them 284 (74,7%) were receiving chemotherapy, 34 (8,9%) immunotherapy, 56 (14,7%) hormonotherapy and 6 (1,6%) concurrent chemo-immunotherapy. Considering immunization, 42,3% had received influenza vaccine, 15,5% pneumococcal vaccine and only 12,1% were immunized for both. For patients receiving chemotherapy regimen, 118 (41,8%) underwent influenza immunization and 47 (16,7%) pneumococcal immunization while the percentages for those receiving immunotherapy were 35% and 15% respectively. Remarkably, 170 (44,7%) of patients were over 65 years of age and nevertheless only 38 (17,6%) of those were pneumococcal immunized. Finally, 8 cases of influenza-like illness were recorded but only half of them have been vaccinated.

Conclusions: Considering these results it is clear that vaccination of oncology patients towards influenza and pneumoniococcus remains low. Subsequently, queries about patients' compliance and health professionals' education are emerging.

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MALIGNANT PERITONEAL MESOTHELIOMA: CASE REPORT

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Introduction: Mesothelioma is a rare but really aggressive neoplasm with poor prognosis, originating from the mesothelial cells of the serosal membrane lining the pleural, peritoneal and pericardial cavities, and the tunica vaginalis. Peritoneal mesothelioma is rare and it accounts for ~10% of all mesotheliomas. It is associated with exposure to asbestos fibers in a subset of patients, typically with a long latency (median ~32 years) but the association seems to be weaker than in pleural mesothelioma. The disease typically presents with non-specific features and tumor nodules of variable size located diffusely throughout the peritoneal cavity, with massive malignant ascites and rare distant metastases.

Aim: The presentation of a rare case of peritoneal mesothelioma diagnosed by cytology of ascitic fluid.

Methods: A 55-year-old male presented with malaise and weight loss since 2 months. Clinical examination and CT demonstrated ascites and multiple peritoneal nodules. Abdominal paracentesis was performed.

Results: The ascitic fluid cytology demonstrated multiple three-dimensional, often papillary-like, groups of neoplastic cells, often scalloped. There was variation in cell size and high nuclear/cytoplasmic ratios, nuclear membrane irregularities and macronucleoli. The cells were positive to WT1, calretinin and CK7 and negative to CDX2, TTF1 and CK20. The diagnosis was peritoneal mesothelioma and was confirmed by the biopsy.

Conclusions: The peritoneal mesothelioma is a rare aggressive neoplasm. It is often hard to be diagnosed. The clinical manifestations (weight loss, malaise, ascites) are usually non specific. It may also mimic radiologically carcinomatosis and has to be differentiated from malignant lymphoma, stromal tumors and tuberculosis. The therapy is most often a combination of cytoreductive surgery and intraoperative hyperthermic chemotherapy. Immunotherapy brings new perspectives (anti-CTLA4 monoclonal antibody and PD-L1 blockade). The 5-year survival rate is 40-60% after therapy.

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PRIMARY MELANOMA OF THE BREAST: EPIDEMIOLOGY AND CLINICAL FINDINGS OF A RARE ENTITY.

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Introduction: Primary malignant melanoma of the breast (PMMB) is a rare, non-cutaneous malignancy of the breast parenchyma, which accounts for less than 0,5% of the breast tumors.

Aim: The aim of this survey is to meticulously review the literature of PMMB and report its epidemiologic and clinicopathologic data.

Material and Methods: Two independent reviewers searched for clinical cases published on PubMed concerning primary melanoma of the breast. Fifteen cases were found, all of which were studied according to their epidemiological, clinical and histological findings.

Results: Regarding these 15 cases, the patients' age varied between 26 to 83 years old and the range of the tumor's size was between 1 to 11 cm. Most of the patients were asymptomatic or they presented with a palpable mass, without any involvement of the skin. The most convincing histological evidence for primary non-cutaneous melanoma is the presence of clustered melanocytes at the mucosal-submucosal junction adjacent to the tumor mass, 43% of which were amelanotic[1]. Diagnostic approach for PMMB is substantiated by fine needle aspiration (FNA) cytology along with immunohistochemistry. The therapeutic approach consists of surgical resection of the tumor along with lymph node dissection in case of nodal involvement. Adjuvant therapy with compounds targeting BRAF and CTL-4 is highly recommended.[2]

Conclusions: The clinical appearance of primary malignant melanoma of the breast is similar to other mammary malignancies such as metastatic melanoma, metaplastic carcinoma and adenocarcinoma of the breast, therefore they should be part of the differential diagnosis. Due to its rarity, our knowledge concerning PMMB is inadequate. Thus, further research is required in order to ameliorate the therapeutic approach and report prognostic data.

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COMPREHENSIVE GENETIC TUMOR PROFILING: APPLICATION IN GREECE, FROM SAMPLE PREPARATION TO CLINICALLY USEFUL RESULT REPORTING

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Introduction: Early cancer diagnosis allows in time medical intervention, significantly improving patient's survival and quality of life. Biomarkers assist in the diagnosis and follow up of tumor development. Basic research has brought in light hundreds of potential cancer biomarkers, more and more of which are introduced in the everyday clinical practice. The primary tumor site is most of the time minute and hard to retrieve material, on which many different analyses have to be performed in order to guide therapeutic decisions.

Aim: Application of a comprehensive genetic tumor analysis for known and emerging cancer biomarkers in single test.

Methods: In 20-40 ng of DNA/RNA from primary and metastatic lesions of solid tumors, we performed Trusight Oncology 500 assay on Illumina NextSeq 500 platform, according to the manufactures' directions. The NGS data were analyzed using the validated PierianDx platform and the results were correlated with the patient's clinical phenotype.

Results: From a total of 25 clinical samples analyzed, 11 were examined only on DNA level for SNVs, In/Dels, CNVs, splice variants, MSI and TMB and the other 14 for the above DNA level variants as well as on RNA level for gene fusions. A total of 130 pathogenic/likely pathogenic variants in known genetic biomarkers were detected that are related with clinically useful information, as well as 175 variations in genes that are not related at the moment with any known pharmacologically useful biologic pathway.

Conclusions: The application of the most comprehensive analysis of the genetic tumor profile using Illumina's Trusight Oncology 500 on primary and metastatic lesions from different cancer types, offers a holistic approach for the identification of known and novel genetic alterations. It comprises the most rational management of the precious and usually limited tumor biopsy material, offering all possible information for existing and emerging diagnostic, prognostic and predictive biomarkers that will allow the clinician to optimally care for cancer patients.

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THE IMPACT OF DEFINITIVE RADIOTHERAPY AND SMOKING CONTINUATION TO PATIENTS WITHT1-T2N0 GLOTTIC CANCER- LATE TOXICITY AND QUALITY OF LIFE. THE EXPERIENCE OF OUR DEPARTMENT

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Introduction: Definitive Radiation Therapy for T1-T2N0 glottic cancer may affects quality of life of patients due to late toxicity as dysphagia and quality of voice disorders.

Aim: To evaluate on retrospectively collected data, the impact of definitive radiotherapy to patients with T1-T2N0 glottic cancer to long term toxicity, as dysphagia and quality of voice disorders, using Voice-Handicap Index (VHI) and also determine correlation with smoking.

Methods: Between 2011 and 2018, thirty two patients with T1-T2N0 glottic cancer treated with radical radiotherapy were retrospectively reviewed. All patients were treated with 3D- conformal RT and received 70Gy with 2Gy per/fraction. The parameters measured were smoking history, T-stage and also anterior commissure (AC) involvement. We determined quality of voice according to questionnaires of Voice Handicap Index 10(VHI). Median follow-up was of 26 months(range 8-84months).

Results: All patients witnessed significant voice improvement following treatment. The incidence of dysphagia grade ≥2 to six and twelve months, was 12.5 % and 8%respectively and patients who suffered had not ceased smoking. Voice quality and communicative ability were satisfying to all patients but slightly worse to patients who continued smoking. Patients who continued smoking had inferior results to VHI than those who had ceased smoking. Also AC involvement and larger RT volumes resulted in poorer voice quality. Patients withT2 tumors experienced worse voice quality before treatment, but voice quality did not remain inferior after RT.

Conclusions: There is a substantial improvement of voice quality after RT. Continuation of smoking has a negative impact on late toxicity and voice quality after RT. Different factors may have specific effects on pre-treatment and post-treatment voice. Advanced RT techniques, better knowledge of tumor biology and function of critical organs involved in speech and swallowing, are necessary to reduce late toxicity and optimize voice quality after RT for early glottic cancer.

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PREDICTIVE VALUE OF A NEW, NON-INVASIVE BIOMARKER, PATRAS IMMUNOTHERAPY SCORE (PIOS), FOR PATIENTS WITH NON-SMALL-CELL LUNG CANCER (NSCLC) TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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Introduction: With the exception of PD-L1 (programmed death-ligand 1) expression and TMB (Tumour Mutational Burden) marker, which have been introduced in clinical practice, no other clinically useful predictive biomarker for immune checkpoint inhibitors (ICIs) has been established so far.

Aim: The aim of the present study was the development of a new, non-invasive and clinically useful biomarker for patients with advanced/metastatic NSCLC treated with ICIs.

Methods: The present study recruited retrospectively and prospectively 112 patients with advanced (stage III and IV) and histologically confirmed NSCLC (adenocarcinoma or squamous cell carcinoma), treated with immunotherapy agents (nivolumab or pembrolizumab) in the Division of Oncology of the University Hospital of Patras. Clinicopathological data, molecular characteristics and response data were collected. Based on clinical parameters, we developed the PIOS (Patras Immunotherapy Score) biomarker in relation to best response (BOR) to ICIs.

Results: Four out of all studied factors that were evaluated -Performance Status (PS), Body Mass Index (BMI), age and lines of treatment (LOT)- were incorporated in the model we developed (PS *BMI/ LOT*age). This biomarker was associated with BOR, with patients having good response [stable disease (SD), partial response (PR) or complete response (CR)] presenting higher levels of PIOS score compared to patients with disease progression (PD) ($p<0.001$). The association remained statistically significant when the 4-tier evaluation (PD, SD, PR and CR) for best response was used ($p<0.001$). The predictive value of PIOS was also validated using binary logistic regression analysis ($p<0.001$). Moreover, PIOS was positively associated with duration of best response ($p=0.019$).

Conclusions: The present study suggests that the PIOS model, which incorporates 4 basic clinical parameters, may allow the selection of NSCLC patients with increased possibility to have clinical benefit from treatment with ICIs.

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CLEAR CELL SARCOMA IN A YOUNG MAN

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Introduction: Clear sell sarcoma is a very rare type of sarcoma. The diagnosis of this subtype of sarcoma is very challenging.

Case report: Male 45 years old.He presented with a non typical skin lesion in the area of left heel in Sep 2019.Initially some focal treatment maybe with ablation or a kind of laser took place by a dermatologist without any improvement.Afterwards, in Oct 2019 a biopsy from that lesion took place and the pathology examination revealed a neoplasm without necrosis, number of mitoses around 3-4 and Ki-67 around 10%. The more possible diagnosis was clear cell sarcoma or malignant melanoma. Further molecular diagnosis in Nov 2019 confirms the diagnosis of clear cell sarcoma with the presence of EWSR1 in approximately 50% of tumors cells (typical 49% and not typical 29%). Moreover, BRAF mutation analysis was negative.Therefore, a proper surgical approach by our plastic surgeons took place in Dec 2019. In particular excision of left calcaneum with sentinel lymph node took place. Pathology examination revealed a neoplasm of 1.3cm max diameter with clear cell sarcoma characteristics. Regarding surgical margins tumor the nearest was 2.2mm. There were multiple small metastatic lesions-infiltrations in the sentinel lymph node the largest one was >2.5mm (without any exocapsic infiltrations). Moreover, in sentinel lymph node some neoplasmatic emboli in veins were found (vascular invasion). Regarding TNM stage it was evaluated as pT1N1Mx by the pathology report.Further and extensive work up with clinical and radiological examinations took place (CT scans, MRIs, Bone-scan and PET-Scan) and was negative for any distant metastases. Additional, due to the close surgical margins a second surgical excision in left heel took place but fortunately the histology examination of new tissue biopsies was negative for any remaining neoplasm or any tumor infiltration. In summary, this gentleman was diagnosed with a Clear Cell Sarcoma of left calcaneum EWSR1 positive that was resected. It is stage IV (T1N1M0) probably G3, without necrosis, number of mitoses around 3-4 and Ki-67 10%, with some vascular invasion and questionable surgical margins in some areas of surgical excision (second surgical excision took place that was negative for any remaining tumor).

Conclusions: Clear Cell Sarcoma is a very uncommon type of sarcomas that should be differentiated from melanoma. The diagnosis sometimes is very difficult and challenging. Molecular diagnosis is recommended.

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MALIGNANT MESOTHELIOMA OF THE PLEURA: A RARE CASE

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Introduction: Mesothelioma is an extremely rare malignant neoplasm, with frequency 1 case/1.000.000/year. It concerns mostly adults aged over 60 years, most often men, although it has been reported also in children. The main risk factor is the exposure to asbestos and the frequency of occurrence in people that have been exposed to asbestos is 300 times higher. It is one of the most malignant neoplasms in humans, with very aggressive biological course and without effective treatment. Most of the patients die in a few months after the moment of diagnosis (mortality 100%). Clinically, it presents with cough, dyspnea, loss of weight, thoracic pain, and malaise.

Aim: The presentation of a rare case of mesothelioma with an emphasis on the differential diagnosis.

Methods: A male patient, 76 years old, came with progressively increasing dyspnea and cough for the last weeks. Imaging revealed nodular thickening of pleura and pleural effusion in the right side. Thoracentesis was performed and we received a specimen from the pleural effusion for cytological examination.

Results: The cytological examination of the smears revealed a population of neoplastic cells consisting of single cells or variously sized three-dimensional aggregations of cells, with sizeable, polymorphous nuclei, nuclear overlapping, and prominent nucleoli. Immunocytochemically, positivity for Calretinin and CK5/6 was revealed, with negativity for TTF-1 and MOC1. These findings were compatible with pleural mesothelioma. Patient underwent chemotherapy and died after few months.

Conclusions: Mesothelioma is a rare aggressive neoplasm with poor prognosis. The prompt diagnosis is crucial. The reactive mesothelial cells are not easily distinguished from the cells of epithelioid mesothelioma, whereas fibrous pleuritis imitates desmoplastic mesothelioma. Mesothelioma is difficult to be distinguished from adenocarcinoma and it should be also distinguished from squamous cell carcinoma. Vascular tumors of the lung may expand in the pleura and imitate mesothelioma. Immunocytochemistry is a useful tool and assists in resolving these diagnostic dilemmas.

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EARLY ESOPHAGUS TOXICITY IN PATIENTS WITH LOCALLY ADVANCED NON SMALL LUNG CANCER AFTER CHEMO-RADIATION THERARY

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Aim: The aim of our study is to evaluated the esophagus acute toxicity in patients with inoperable non small lung cancer after chemotherapy and radiotherapy.

Methods From January 2012 to Dicembre 2018,187 patients with locally advanced non small lung cancer received in our department radiotherapy and chemo-therapy. The median age was 62 years. From these patients 119 had received sequential chemo-radiation therapy ,initially three cycle of chemotherapy (cisplatin/gemcitabine)and then radiotherapy and 68 patients received concurrent chemo-radiotherapy (cis-platin). The total dose of radiotherapy was 60Gy(3-D CONFORMAL RT).The early esophagus toxicity has been evaluated according the RTOG/EORTC criteria

Results: The grade I toxicity(Mild dysphagia or odynophagia / may require topical anesthetic or non-narcotic analgesics / may require soft diet) was ranged in the same level in the concurrent chemo-radiotherapy and the sequential chemo-radiotherapy (41%% versus 44%).The grade II toxicity (Moderate dysphagia or odynophagia / may require narcotic analgesics / may require puree or liquid diet) was 27% for the sequential and 29% to the concurrent. But the grade III toxicity (Severe dysphagia or odynophagia with dehydration or weight loss > 15% from pretreatment baseline requiring NG feeding tube, IV fluids, or hyperalimentation) was 2% for the sequential chemo-radiotherapy and 18% for the concurrent chemo-radiotherapy.Only one patient had grade IV toxicity(Complete obstruction, ulceration, perforation, fistula).
The concurrent chemo-radiation is the most important factor for the early esophagus toxicity ,but there is another dosimetrical factor that increase the toxicity ,the volume of esophagus that received 35 Gy .Our results seems that the esophagus toxicity was bigger when the irradiated volume of esophagus was bigger(V50<32 Gy).

Conclusions: The grade of the early esophagus toxicity in patients with locally advanced non small cell shows that it is significantly burdened, from the concurrent chemo-radiotherapy and the total volume of the irradiated esophagus.

OVARIAN FIBROMA IN A 58-YEAR OLD PATIENT: CYTOLOGICAL DIAGNOSIS OF AN INTERESTING CASE

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Introduction: Sex-cord tumors – tumors of the ovarian stroma - come from the developing gonad and respectively from the primitive sex cords or the specialized ovarian substrate. They concern 8% of all the primary ovarian neoplasms. Fibromas are rare, compact, benign tumors of ovarian stroma, which represent 1% - 4% of all benign ovarian tumors. They are usually unilateral, 1 to 10 centimeters in diameter and they appear in women aged from 20 to 80 years.

Aim: The presentation of interesting case of fibroma, which was diagnosed cytologically, in 58-year old patient.

Methods: A female patient 58 years old came with persistent abdominal pain for the last weeks. Her history was free. Imaging revealed a compact lesion in the left uterine appendage, with some cystic features, the biggest of them 14 cm in diameter. Patient underwent total hysterectomyand bilateral salpingo-oophorectomy. For cytological examination, we received liquid from the cystic part of the lesion.

Results: The cytological examination of the smears revealed aggregations of medium-sized cells, with ovular or circular nuclei, nucleoli, thin chromatin, with partial nuclear overalapping and a little of cytoplasm. Sparse spindle-shaped cells with regular nuclei were also observed. The immunocytochemical assessment showed positivity for Vimentin and Calretinin. These findings were compatible with ovarian fibroma and the diagnosis was confirmed furtherly with the histological diagnosis.

Conclusions: Ovarian fibromas are rare, benign neoplasms which are treated surgically. Prognosis is excellent, and the recurrences concern more the cellular fibromas. They have a remarkably interesting differential diagnosis and they should be distinguished from leiomyomata and mainly from other malignant neoplasms of the ovary, which they imitate clinically and radiologically. The cytological examination in combination with immunocytochemistry isa precise and reliable diagnostic method. The histological examination confirms the diagnosis.

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ANAPLASTIC THYROID CARCINOMA: A RARE CASE

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Introduction: Anaplastic thyroid carcinoma (ATC), though rare, is the most aggressive form of thyroid cancer. It originates from the follicular cells and it seems that the most "sarcomatoid" thyroid tumors are anaplastic carcinomas. It comprises only the 2-5% of the malignant thyroid tumors but is responsible for more than 50% of deaths due to thyroid cancer. It is usually a rapidly growing neck mass that infiltrates the surrounding tissues. It is more common in women (f:m 2:1) and in older ages. There are three histologic patterns, singly or in combination: giant cell, sarcomatoid and epithelial .

Aim: The presentation of a rare case of anaplastic thyroid carcinoma in a male patient.

Methods: A 89-year-old male presented with dyspnea and voice hoarseness since a month. Clinical examination demonstrated a large, firm, ill defined neck mass. Ultrasound revealed diffuse enlargement of the right lobe which was almost totally replaced by an hypoechoic mass of about 6cm. FNA was performed.

Results: The smears were cellular comprising of pleomorphic cells arranged in clusters, diffusely or singly scattered. The cells were large, with round to oval nuclei, coarse chromatin, prominent nucleoli and moderate to abundant cytoplasm. Few bizarre cells were observed. The background was inflammatory and focally necrotic. The diagnosis was anaplastic thyroid carcinoma.

Conclusions: The anaplastic thyroid carcinoma is a rare but very aggressive tumor. The patients usually have distant metastases at the time of diagnosis (30-40% lung, brain, bones). Treatment of anaplastic thyroid carcinoma (ATC) is mostly palliative. Surgical resection with adjuvant radiation therapy and chemotherapy may prolong survival somewhat and improve quality of life. The median survival is about 6 months. FNAC is important for the right diagnosis.

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A SINGLE-CENTER RETROSPECTIVE ANALYSIS OF PATIENTS WITH TESTICULAR CANCER FROM 2010-2019

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Introduction: Testicular cancer is the most common malignancy among men aged 18 to 39. The main symptom leading to diagnosis is testicular pain, followed by lower back pain and dyspnea. Ten-year survival is as high as 95%, even in case of advanced disease, due to high response rates to chemotherapy (BEP, VeIP, TIP). Since the 1980's, no new drugs have been introduced for the management of the disease. However, we now have data supporting the administration of fewer cycles of chemotherapy in patients with stage I disease.

Aim/Methods: Data was collected retrospectively from 125 patients diagnosed with testicular cancer from 2010 to 2019 and treated in our clinic. The age at diagnosis ranged from 18 to 63 years. 59 of the patients (47%) had cancer of the right testicle, 66 (53%) of the left testicle, and 5 of both testicles. 46 (36%) were seminomas, 76 (58%) were non-seminomas, and for 6% no data was recorded.

Results: Most patients were diagnosed at stage I (64 patients), with fewer at stage II (48) and III (17). Patients with stage I non-seminomas received BEP for 2 cycles (32), EP for 2-3 cycles (2), or BEP for 1 cycle (1). Patients with stage I seminomas received no chemotherapy (14), carboplatin for 2 cycles (10), carboplatin for 1 cycle (1), or radiotherapy (1). Some patients with stage III disease received chemotherapy prior to surgery based on tumor marker levels; in 5 of them no evidence of disease was found when the surgery was performed. To date, recurrence of the disease was seen in only 8 out of all the patients. All of them received treatment, including surgery in some cases, and only two died because of the disease.

Conclusions: The data collected over the past decade from patients in our clinic in Northern Greece confirm the effective management of testicular cancer and the high survival rates.

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PLATELET VALUE AND PROGNOSIS-RESPONSE TO 1ST LINE THERAPY IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Introduction: The 5-year survival rate for patients diagnosed with lung cancer is below 20% even nowadays. The prognostic role of platelet value hasn't been fully clarified in this group of patients.

Aim: The purpose of this study was to investigate the connection between platelet count and the response to 1st line therapy, as well as the prognosis, for advanced non-small cell lung cancer (NSCLC).

Methods: 40 previously untreated patients with stage IV NSCLC were divided into two equal groups according to their platelet status. Thrombocytosis was defined as platelet counts $\geq$ 450.000/mm^3. We collected clinical parameters and the value of platelets at three different time points: before chemotherapy, at the evaluation of the disease and after progression. The results were correlated with Progression-Free Survival (PFS) and Overall Survival (OS) using univariate and multivariate Cox proportional hazards regression models and Kaplan-Meier analysis.

Results: Patients with normal platelets had a median PFS of 7,8 months, while median PFS was 8,3 months for the group of patients with thrombocytosis. This difference was not statistically significant. Median OS for the two groups was 18,7 and 18,5 months respectively, but there was no statistically significant difference, either. Multivariate survival analyses demonstrated that bone or adrenal metastases were independently associated with disease progression. Finally, adrenal metastases were the only independent prognostic variable.

Conclusions: The present study showed that platelet count cannot be used as a predictive and prognostic marker for our patients. However, further larger studies are needed to evaluate the precise prognostic significance of this parameter for the treatment of NSCLC.

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THERAPEUTIC APPROACH AND LONG-TERM SURVIVAL OF A PATIENT WITH METASTATIC PROSTATIC DUCTAL ADENOCARCINOMA: CASE REPORT

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Introduction: Prostatic ductal adenocarcinoma (PDA), even though it is the second most common histological subtype, accounts for only 0.4% -0.8% of prostate carcinomas. It usually has a more aggressive biological behavior associated with low resectability and a greater tendency for visceral metastases. Hormonal therapy seems to be effective, and there are literature reports describing a shorter duration of response to docetaxel, as well as data concerning three patients with metastatic PDA who received gemcitabine / cisplatin with good response to this treatment.

Aim: The description of a patient case with prostatic ductal adenocarcinoma and long-term survival as well as the review of bibliographic data concerning the therapeutic approach for these patients.

Case: A 60-year-old patient with PDA, Gleason score 8 (4 + 4), microsatellite stable, BRCA wt, with lung and bone metastases since 7 years, initially was offered androgen deprivation therapy, but due to rapid disease progression he was treated with docetaxel, with a subsequent drop in PSA level and imaging stabilization lasting more than one year. Further hormonal manipulations were performed with bicalutamide and enzalutamide without a good response. He then received consecutively 10 cycles of cabazitaxel, 6 cycles of docetaxel and 8 cycles of paclitaxel / carboplatin, showing good tolerability, clinical and imaging improvement. Afterwards, due to gradual imaging progression of the disease and lack of treatment options, he was offered mitoxantrone and again docetaxel and cabazitaxel. After neuroendocrine differentiation of the disease was ruled out, treatment with gemcitabine / cisplatin was finally started, based on 3 case reports describing its effectiveness in PDA. The patient received a total of 7 cycles, showing a continuous response and reduction of tumor burden by 60%. Since the last 3 months he has been taking a treatment break and remains in good condition, having only mild peripheral neuropathy.

Conclusion: The metastatic PDA seems to respond to chemotherapy based on taxanes as well as to the combination of gemcitabine / cisplatin, with potentially long-term survival.

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HEPATOID LUNG ADENOCARCINOMA: A RARE CASE

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Introduction: Hepatoid carcinoma is an exceedingly rare type of malignant tumor, which histologically is similar to hepatocellular carcinoma. It is defined as an adenocarcinoma with typical glandular or papillary formations and features of hepatoid differentiation and expression of alpha-FetoProtein (AFP). The tumor cells show a centrally located nucleus and abundant eosinophilic cytoplasm, similar to the cells of hepatocellular carcinoma. It is localized more usually in the stomach (63%), following the ovary (10%0, the gallbladder, pancreas, and endometrium. The development in the lung is extremely rare, with 22 reported cases in international bibliography. The majority of the patients were males, smokers and the disease was diagnosed in an advanced stage.

Aim: Presentation of a rare case of hepatoid adenocarcinoma of the lung in a female patient.

Methods: A female patient 50 years old came to our hospital reporting non-productive cough. Radiology revealed atelectasia of the right lower lobe, small pleural effusion ipsilaterally and enlarged lymph nodes were revealed, of antecarinal and subcarinal region. EBUS-TBNA was performed (endobronchial ultrasound guided transbronchial needle aspiration) and a sample was collected for cytological examination.

Results: The cytological examination of the smears of the transbronchial needle aspiration from a mediastinal lymph node (RLN4) revealed aggregations of tumor cells with sizeable nuclei with polymorphism, coarse chromatin, frequent nucleoli, and abundant cytoplasm. Immunocytochemically, positivity of tumor cells was observed for TTF-1 (cytoplasmic), CK7 and AFP and negativity for CK5/6, CK20, p63 and CDX2. The above findings in correlation with the clinical data (no findings in the gastrointestinal tube / liver) were compatible with metastatic infiltration of lymph node by hepatoid lung carcinoma.

Conclusions: Hepatoid lung adenocarcinoma is an extremely rare neoplasm with aggressive biological course and frequent liver metastases. In the differential diagnosis metastatic hepatocellular carcinoma is firstly included and its distinction could be difficult, especially in patients with sites in the lungs and the liver. Also, metastasis from stomach should be excluded. The combination of clinical, radiological, and cytological – histological findings and obviously the immunocytochemistry-immunohistochemistry lead to the correct diagnosis.

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IDENTIFICATION OF PREDICTIVE FACTORS FOR THE OXALIPLATIN INDUCED NEUROPATHY IN PATIENTS WITH COLON CANCER

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Introduction: The colorectal cancer is the third most frequent cancer at men and the second at women. The oxaliplatin is used in the adjuvant therapy and also in the metastatic disease at the chemotherapeutic combinations FOLFOX and XELOX. The incidence of the acute peripheral neuropathy caused by oxaliplatin is between 4% and 98%. Also the incidence of chronic neuropathy is about 70%.

Aim: This research attempted to lighten the relation between the oxaliplatin induced peripheral neuropathy and the mutation status of ras gene, the blood's serum levels of the magnesium, the calcium, the sodium, the potassium, the haemoglobin, the albumin, the transaminases, the uric acid and the LDH. Also evaluated the relation of the neurotoxicity of the oxaliplatin and the GFR, the ejection fraction, the age, the sex, the stage of cancer and the cumulative dose of oxaliplatin of the patients.

Methods: This retrospective research included 39 patients, who treated with FOLFOX in the First Department of Clinical Oncology of Theageneio Anticancer Hospital. The evaluation of neurotoxicity based on NCI-CTCAE criteria. The univariate statistical analysis of the quantitative variates was conducted using the t-tests or the Mann–Whitney U test. For the clinical categorical variates was used the x2 test. The multivariate analysis followed using logistic regression model.

Results: From the univariate analysis was concluded statistically significant correlation of the oxaliplatin's neurotoxicity with the uric acid of the blood serum (p:0.042), especially when the uric acid is more than 5.3 mg/dl (p:0.037), the serum albumin less than 4.3 gr/dl (p:0.034), the total number of the cycles of the chemotherapy (p: 0,022) and the ejection fraction (p: 0.003), especially when the EF is lower than 60% (p:0.012). At the multivariate analysis the statistical significance was reserved for the uric acid (OR 8.80) and the ejection fraction (OR 0.095).

Conclusions: The oxaliplatin's induced neuropathy is associated with the pre-chemotherapy increased levels of the blood serum's uric acid and with the decreased ejection fraction.

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PREDICTIVE FACTORS IN IMMUNOTHERAPY

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Introduction: Immunotherapy has emerged as the core of oncology treatment. Nonetheless, only a subset of patients derives clinical benefit, emphasizing the need to use predictive biomarkers; many of these biomarkers (i.e. PDL1, MSI, TMB) rely on tissue, limiting their use in daily practice. Measurements of routine blood markers such as CRP or neutrophil to lymphocyte ratio have spurred interest for their potential prognostic value and ease of use.

Aim & Methods: The purpose of this study was to identify useful biomarkers from our daily clinical practice. From 2016 to 2019, a total of 146 patients with various types of neoplasms, who have received immunotherapy, were identified from the archives of the University Hospital of Ioannina (PGNI). We retrospectively recorded age, sex, pathological diagnosis, stage, line/type of immunotherapy, autoimmune diseases, allergies or infections at baseline, survival data (OS & PFS), response, LDH, calcium, albumin levels and complete blood count to identify prognostic or predictive factors.

Results: In the present study we present our experience from the use of immunotherapy in the Oncology Department of the University hospital of Ioannina and we examine the prognostic and predictive utility of simple clinical and laboratory parameters.

Conclusions: Biomarkers with strong predictive and prognostic value, in addition to guiding clinical trial design, will be critical to individualize immunotherapy in clinical practice.

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SPINAL CORD COMPRESSION DUE TO EXTRAMEDULLARY HEMATOPOIESIS IN A PATIENT WITH BETA-THALASSEMIA, TREATED WITH RADIOTHERAPY. A RARE CLINICAL PRESENTATION AND REVIEW OF RECENT LITERATURE

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Introduction:	Extramedullary hematopoiesis is a common occurrence in patients with severe beta-thalassemia. Most often it affects organs such as the liver, spleen and lymph nodes. It is rarely met in the vertebral column. It is observed primarily in the thoracic spine and then in the lumbar spine. A not-so-common consequence of this is compression of the spinal cord due to hematopoiesis foci and subsequent neurological symptoms.
Aim:	Presentation of the clinical, laboratory and imaging findings and treatment of spinal cord compression due to extramedullary hematopoietic foci in a patient with beta-thalassemia.
Methods:	We reviewed the recent literature on this clinical entity in the PubMed / MEDLINE database until 12/2019.
Results – Case Report:	A 53-year-old man presents with progressively worsening gait and instability. The patient has a history of beta-thalassemia, for which he receives blood transfusions every 15 days, while since 1988, foci of extramedullary hematopoiesis have been found in the region of thoracic spine and for which he underwent transfusions from 1994 to 1996 and radiotherapy sessions in 1996 due to their increase and instability of gait and spinal cord pressure. Since then, the patient has remained stable without the need for new sessions. Recurrent symptoms have been reported in the last year (gait instability, sphincter dysfunction and difficulty in climbing up stairs). In a new imaging test with MRI of the thoracic and lumbar spine, an increase in the size and number of foci was shown. It was initially treated with transfusions, corticosteroids and analgesics. Due to the worsening of the pain, he finally underwent new sessions of radiotherapy in the area (L5-S1).
Conclusions:	The treatment of this rare clinical entity can be achieved through transfusions, surgery, radiotherapy or a combination of all of the above. There is no agreement on the total dose of radiation therapy and the doses range from 20-30 Gy, with a daily dose of 2-3 Gy.

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INTRADUCTAL PAPILLARY NEOPLASM OF THE BILE DUCTS (IPNB): A RARE CASE

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Introduction: Intraductal papillary neoplasm of the liver and the bile ducts is a rare neoplasm, representing 10 – 15% of the bile duct tumors. It is characterized as a macroscopically visible, pre-cancerous lesion, with papillary or villous architectural pattern of dysplastic epithelium inside the intrahepatic or extrahepatic bile ducts and mucin production. The mean age of occurring is 50 -70 years. Histologically, it is characterized by papillary structures, with thin fibrovascular cores, which are covered by intestinal, pancreatobiliary, gastric or oncocytic type of epithelium. According to WHO classification it is classified in papillary neoplasms with low- or high-grade dysplasia, with coexisting infiltrative component.

Aim: The presentation of a rare case of intraductal papillary neoplasm of intrahepatic biliary ducts.

Methods: A female patient, 81 years old came with pain in the lower right abdomen. By the laboratory examinations, increased CA 19-9 was observed. Ultrasound imaging revealed a focal, oval-shaped, relatively hyperechoic lesion with halo, in the right lobe of the liver, which was aspirated.

Results: The cytological examination of the smears of the aspiration sample revealed the presence of complex three-dimensional papillary formations, with frequently visible thin fibrovascular cores. The epithelial cells showed severe dysplasia, with dark-colored or frequently clear nuclei, thickening of the nuclear membrane, visible nucleoli and mucinous vacuolation of the cytoplasm. The above presented findings in correlation with the radiological findings were suggestive for intraductal papillary neoplasm of the intrahepatic bile ducts, with moderate to severe dysplasia. The diagnosis was confirmed by the histological examination of liver biopsy. Patient died because of bad general condition before the performance of the surgical procedure.

Conclusions: IPNB is a rare entity, especially in Western countries, which increases the risk of development of cholangiocarcinoma and it is included in "precursor lesions". The sequence of carcinogenesis includes a lot of mutations concerning common pathways of oncogenesis (KRAS, loss of p16 and mutation of TP53). It is treated with surgical excision and histological examination of the specimen, in order to exclude the infiltrative cholangiocarcinoma, which frequently coexists and worsens prognosis.

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PREVALENCE OF IMMUNOTHERAPY RELATED HYPOPHYSITIS: A RETROSPECTIVE STUDY

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Introduction: Immunotherapy with checkpoint inhibitors has changed the treatment of many cancers, but often present adverse events (AE) that affect many organs. Among these, endocrine AE is common. CTLA-4 inhibitor ipilimumab alone or in combination with PD-1 inhibitors can cause pituitary insufficiency with impaired pituitary hormone secretion at 3.2% and 6.4%, respectively. While PD-1 and PDL-1 inhibitors rarely cause hypophysitis up to 1%.

Aim: To highlight the prevalence of hypophysitis as an AE of immunotherapy and its clinical significance.

Methods: Retrospective study of patients who received immunotherapy from March 2018 to January 2020 at the Second Department of Medical Oncology, St Savvas Anticancer Hospital. Epidemiological, clinical and laboratory were analyzed.

Results: 55 patients were studied (33 men, mean age 66.5 years, range 37-85). 40% had lung cancer, 29.1% melanoma, and 12.7% urethral cancer. 83% had metastatic disease. Of the 55 patients, 28 (50.9%) received immunotherapy with pembrolizumab, 21 (38.2%) with nivolumab, 4 (7.3%) with durvalumab and 2 (3.6%) with a combination of ipilimumab and nivolumab. The median treatment time was 7.23 months (range 1-28). A total of 5 patients out of 55 who received immunotherapy (9%) presented with hypophysitis based on laboratory tests: 2/28 (7.1%) with pembrolizumab, 1/2 (50%) with a combination of ipilimumab and nivolumab, and 2/21 (9.5%) with nivolumab. No patients presented clinical manifestations. All of them, were treated with hydrocortisone or prednisolone and continued to receive treatment with close endocrinologic monitoring. Statistical analysis of epidemiological, clinical and laboratory data demonstrate no predictive factors for the development of hypophysitis.

Conclusions: In our study, the prevalence of hypophysitis is 9%. None of the patients had clinical symptoms and all of them continued to receive immunotherapy with close endocrinologic monitoring and appropriate hormone replacement therapy.

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NEUROENDOCRINE TUMOR OF UNKNOWN PRIMARY ORIGIN AND MEN-1 SYNDROME

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Introduction: NeuroEndocrine Neoplasms (NENs) have been characterized as rare neoplasms. NETs are epithelial neoplasms with prominent neuroendocrine differentiation and can develop in any tissue. The histological, molecular and imaging features of NETs are in general indicative of the primary origin, yet in some cases the detection of primary side can be very challenging.

Case report: 42-year-old male with a past medical history of Multiple Endocrine Neoplasia type 1 (MEN 1) presented with an anterior mesothorasic mass and a second one in the inferior cervical region. The lesions were identified during the work-up which followed a pancreatic surgery. Particularly, patient was diagnosed with primary hyperparathyroidism and nephrolithiasis 20 years ago and underwent sequential excision of three parathyroid glands. Due to family history of primary hyperparathyroidism further and extensive work-up took place, which revealed the presence of MEN 1 syndrome. Molecular diagnoses detected the presence of the likely pathogenic p.A541T mutation and radiological examinations depicted two large pancreatic masses. Therefore, a segmental pancreatecomy, splenectomy and a cholecystectomy (due to chololithiasis) took place. The pathology examination revealed infiltration of well differentiated NET, grade2 (NETG2WHO,2MF/10HPF, Ki-67=5%), chromogranin, synaptophysin, PGP9.5 and CD56 positive. Postoperatively pancreatic pseudocysts occurred, which were treated with proper surgical approach (trans-gastric drainage). As a result of pancreatectomy, a mild diabetes mellitus was detected and treated with metformin. Additionally, MRI scan of pituitary gland revealed a small adenoma 2mm, stable in size without secretion of hormones. Patient underwent a thoracoscopic biopsy of the mesothorasic mass and a fine-needle aspiration biopsy of the cervical mass. The pathology examination revealed neuroendocrine tumor, grade2 (NETG2WHO,0MF/10HPF, Ki-67=25%), chromogranin, synaptophysin positive, as well as positive in CD56 and Bcl2, and partially positive in pankeratin AE1/3.

Conclusions: MEN syndromes are rare. Most of the time, acquiring a proper medical history (individual and family) may reveal the presence of MEN. Molecular diagnosis is essential and medical treatment in specialized centers is recommended.

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HR+/HER2- ADVANCED BREAST CANCER: REAL WORLD USE OF ABEMACICLIB IN UCLH (UNIVERSITY COLLEGE LONDON HOSPITAL) BREAST UNIT

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Introduction: Hormone receptor-positive advanced breast cancer comprises the majority of breast cancer (BC) cases and is preferably treated with endocrine therapies except in cases of visceral crisis. The addition of CDK4/6 inhibitors to standard endocrine treatment in the metastatic setting is currently the golden standard. In Greece, the CDK4/6 inhibitors Palbociclib and Ribociclib are used, but there is limited experience with the Abemaciclib.

Aim: In this abstract, we aim to present real-world data from the use of abemaciclib with either an aromatase inhibitor or fulvestrant for patients with metastatic BC treated in a tertiary cancer centre in the UK.

Patients and methods: We collected retrospectively individual patient's data for 19 women (aged 41-90) from electronic medical records. Patients were treated between April 2019 and February 2020 (follow up time was ten months). 3/19 were premenopausal and received goserelin 4-weekly concurrently. 7/19 patients had abemaciclib with AI as first-line treatment, 6/19 as second-line and 6/19 as third line with fulvestrant. Patients characteristics: 12/19 had visceral metastases (liver, lung), one of them had brain mets, and one patient had meningeal disease, whereas 6/19 had bone-only disease. 5/19 patients had primary endocrine resistance (relapsed while on the first 2 years of adjuvant ET or PD within 6 months of first-line for advanced BC), and 4/19 had Gr.3 disease. 5/19 patients had been previously treated with chemotherapy in the metastatic setting.

Results: 16/19 patients had disease control (PR or SD) and 12/19 are still on the treatment. Maximum duration time is ten months. Fatigue gr I, II (12/19) and diarrhoea gr I, II, III (10/19) were the most frequent adverse events. Other AEs were hepatotoxicity gr II (1/19), mucositis gr II (1/19) and neutropenic fever that required hospitalization (2/19). 2/19 patients discontinued treatment due to toxicity (neutropenia and acute kidney injury), 9/19 reduced dose to 100mg x 2 and 2/19 reduced to 50mg x 2. 6/19 patients tolerated reasonably well the initial dose. Diarrhoea was controlled with dose modifications. Although fatigue was a cumulative side effect that occurred later than diarrhoea, it was not resolved with dose reduction.

Conclusions: The abemaciclib in daily clinical practise has been proven effective in high-risk patients with high-grade tumours, visceral disease and endocrine resistance while the toxicity was manageable. The effectiveness and toxicity profile were in accordance with the results from MONARCH – 2 and -3 clinical trials. Despite the small numbers, this patient cohort represents a real-life population suggesting that the Abemaciclib is a safe and effective treatment option for patients with advanced HR+/Her2- BC.

Abbreviations: BC: breast cancer, AE: adverse event, AI: aromatase inhibitor, ET: endocrine treatment

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RECCURENT ADENOCARCINOMA OF THE PANCREAS. GOING THROUGH THE LIMIT.

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Introduction: The adenocarcinoma of the pancreas is the 4th cause of overall deaths due to cancer. The overall survival declines in association with the TNM tumor's staging, something that happens at the recurrence after a definite surgery, as well. There are no many published references about the management of cases like that. Herein, we describe a case of constantly recurrent, locally, adenocarcinoma of the pancreas that has overcome the expected five year overall survival.

Aim: The aim of this reference is to highlight the importance of surgical excision at the local recurrences.

Methods: A 55 years old man, without any medical record, after a medical investigation due to dyspepsia and abdominal pain, found to suffer from an adenocarcinoma of pancreas. At the computed tomography revealed a mass of the body to tail of pancreas, that it was characterized as inoperable. The patient started with 'neoadjuvant' chemotherapy (FOLFOXIRI regimen) with the aim to make the tumor operable. After the completion of the systemic treatment the patient underwent a peripheral pancreatectomy with splenectomy. He received adjuvant systemic chemotherapy with Gemcitabine/Abraxane. Twelve months post-surgery, the tumor relapsed and the patient received radiotherapy and chemotherapy with capecitabine. A year after he had a second relapse locally and the patient underwent a total pancreatectomy with partial gastrectomy. After that the patient is free of disease.

Results: As long as, there are no guidelines for this small subgroup of patients, there is not a gold standard approach for a patient with a locally recurrent adenocarcinoma of pancreas, especially if there are more than one recurrences. From the describing case, we could assume that a more aggressive treatment with the aim of the excision of the recurrent disease, could be a good way of dealing with cases like that, trying to achieve the most of overall survival.

Conclusions: The patients with locally recurrent adenocarcinoma of pancreas after surgery, form a unique, rare subgroup of the patients with pancreatic neoplasms. There are no trials, or evidence of the best management of these patients, so the surgical excision of the recurrence seems to be the best way of treating with the aim of prolongation of recurrence or progression free survival and overall survival.

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IMMUNOTHERAPY VERSUS CHEMOTHERAPY FOR PREVIOUSLY TREATED METASTATIC NSCLC. RESULTS FROM DAILY CLINICAL PRACTICE

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Introduction: Immunotherapy is based on the activation of our immune system, against tumor cells, and has shown impressive results in the NSCLC treatment, initially in the 2nd line therapy, and then, in the 1st line setting. In the 1st line setting, it was initially used as monotherapy, and lately in combination with classic chemotherapy regimens.

Aim: The aim of this retrospective analysis is to compare both the efficacy as well as the toxicity of chemotherapy and immunotherapy in the 2nd line treatment of mNSCLC.

Methods: Fifty-nine patients, consecutively admitted in our Medical Oncology Department were enrolled in our study. 83% men, 17% women, of median ECOG 1 (0-3), median age 68 (47-86) years, stage V squamous (32%) and non-squamous (68%) histology, were treated with 1st line chemotherapy regimens. Following disease progression, they received 2nd line therapy, either chemotherapy or immunotherapy. We compared both the efficacy and toxicity of the two 2nd Line therapy options. In the immunotherapy arm, patients received either Nivolumab, or Pembrolizumab.

Results: The number of patients whose disease progressed after receiving chemotherapy in the 2nd line, was similar to those that received immunotherapy. However, time to progression, was significantly shorter in the chemotherapy arm ($p=0,015$). There was significant difference in disease progression probability between the two arms in both 3 and 6 months ($p<0,05$). Patients with at least one adverse effect, had 2,27 times higher probability of disease progression. Median overall survival was 8 months for the chemotherapy arm in second line, compared to 14 months in the immunotherapy arm. There was no difference in survival between the two arms in the 6 months evaluation ($p>0,05$). However, in the 12 and 18 months evaluation, survival rates were significantly higher for patients in the immunotherapy arm ($p=0,006$ και $p=0,001$ respectively).

Conclusions: Patients who received immunotherapy in 2nd line, had siginificantly higher overall survival rates, compared to those that received chemotherapy ($p=0,006$). There was no correlation between PD-L1 expression levels and clinical benefit. Immunotherapy showed less toxicity than chemotherapy. Data from our daily clinical practice are in line with current literature.

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R0 PANCREATECTOMY INCIDENCE IN THE LAST DECADE, THE EXPERIENCE OF THE UNIVERSITY HOSPITAL OF LARISSA

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Introduction: Accurate estimation of R0 pancreatectomy incidence is of great importance in pancreatic cancer treatment, as such excisions are correlated with higher 5-year survival rates. Despite the lack of a globally accepted definition of R0 pancreatectomy, a realistic estimation of its incidence will be attempted, via the use of the most recent diagnostic protocols.

Aim: The presentation of the histopathological findings and the accurate estimation of R0 pancreatectomy incidence in our hospital.

Methods: Forty-nine (49) histopathology reports from patients who underwent pancreatectomies performed during the last decade (2010-2019) were evaluated. Relevant literature from the MEDLINE/pubmed website were also evaluated.

Results: After thorough examination of the available reports, an incidence of 81,6% of R0 pancreatectomies was calculated. This percentage is in compliance with global rates, which fluctuate from 20% up to 85%, owing to discrepancies in R0 pancreatectomy definition worldwide.

Conclusions: R0 pancreatectomy incidence, as calculated by examination of histopathological data, is in compliance with national trends. The prominence of R0 pancreatectomies is correlated with better prognosis and higher survival rates. However, the adoption of a globally accepted definition should be a high priority, so as the available research data and conclusions become more reliable.

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METASTATIC NEUROENDOCRINE CARCINOMA OF THE CERVIX TREATED WITH PDL1 INHIBITOR, NIVOLUMAB.

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Introduction: Neuroendocrine carcinoma of the cervix is a rare aggressive form of cervical cancer, about 2% of cases. It is characterized by a high frequency of lymph node metastases and early hematogenous dissemination. Human papillomavirus (HPV) appears to be the main causative agent. The prognosis is unfavorable and there is no standard treatment based on clinical studies.

Aim: We present a clinical case with PDL-1 negative metastatic neuroendocrine cervical carcinoma heavily pretreated that received treatment with Nivolumab and experienced immediate radiographic response and clinical improvement of symptoms.

Presentation of case: A 72-year-old women was diagnosed with metastatic neuroendocrine carcinoma of the cervix. Initially the disease extended with a lesion 20 x 17 cm to the pelvis, a mass 4 cm to the left adrenal gland, a lymph node block 4 cm to the Haler tripod and a single lesion 1.5 cm to the liver. She treated with Etoposide (100 mg/m^2 IV on day 1, 2 and 3) and Cisplatin (80 mg/m^2 IV on day 1) and a partial response was recorded. Few months after and due to vaginal bleeding she underwent urgent total abdominal hysterectomy with bilateral salpingo-oophorectomy. Relapsed 6 months later with enlargement of the adrenal gland mass and we preferred to re-challenge her with Etoposide and Cisplatin chemotherapy and we achieved again a partial response. Subsequently due to disease progression received 3rd line treatment with Topotecan (0.75 mg/m^2 IV on day 1, 2 and 3) and 4th line treatment with Paclitaxel (135 mg/m^2 IV on day 1) and Carboplatin (AUC 4 IV on day 1). The patient is receiving hydrocortisone replacement therapy due to adrenal insufficiency as a result of adrenal masses. Finally, after approval, she received treatment with Nivolumab at a dose of 3 mg/kg IV every 2 weeks and after 6 cycles a significant decrease of all target lesions was recorded and great relief of symptoms. Molecular characterization of her tumor showed absent PD-L1 expression.

Conclusions: Immune checkpoint inhibitors may be active in cervical neuroendocrine carcinoma with the probability of benefit in some patients regardless of PDL-1 status.

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THE EFFECT OF CHEMOTHERAPY AND RADIOTHERAPY IN PATIENTS WITH METASTATIC NON-SMALL-CELL LUNG CARCINOMA (NSCLC) TREATED WITH IMMUNOTHERAPY. A RETROSPECTIVE STUDY OF THE MEDICAL ONCOLOGY DEPARTMENT AT THE UNIVERSITY HOSPITAL OF IOANNINA

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Introduction: Although immunotherapy is a promising treatment strategy on the management of patients with metastatic NSCLC, there are subsets of patients that do not respond or become resistant to treatment. Chemotherapy (Ch) and radiotherapy (RT) may increase the benefit of immunotherapy. We aimed to investigate the effect of prior chemotherapy or radiotherapy on patients with metastatic NSCLC who received immunotherapy in our Department.

Patients and Methods: We investigated the data from 68 patients with metastatic NSCLC managed in our Department in the period from 01/2016 to 06/2019 and were treated with immunotherapy. The Overall Survival (OS) and Progression Free Survival (PFS) were estimated from the date of diagnosis. The statistical analysis was performed by using the *SPSS package IBM version 25*.

Results: 57.1% of patients had Adenocarcinoma and 33.3% had Squamus Cell Carcinoma. 97% were smokers, while a genetic mutation was detected in 17% of patients. Patients that had received radical RT in the past had better OS as compared with patients that received palliative or no RT (HR:0.162, p=0.016 και HR:0.178, p=0.027 respectively). The number of previous chemotherapy treatment lines did not have any effect on OS in patients that received immunotherapy. However patients that received immunotherapy in the first line had better PFS as compared to patients that received immunotherapy in latter lines (HR: 0.23, P:0.045).

Conclusions: Prior radical RT had a positive effect on the OS of patients with metastatic NSCLC treated with immunotherapy. A possible abscopal effect may be related with this observation that needs prospective validation.

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PIGMENTED VILLONODULAR SYNOVITIS (PVNS) IN KNEE JOINT – RADIOTHERAPY. CLINICAL CASE PRESENTATION AND REVIEW OF THE RECENT LITERATURE

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Introduction:	Pigmented villonodular synovitis (PVNS) is a rare, idiopathic, benign, but potentially locally aggressive, recurrent clinical entity. It is characterized by hyperplasia, deposition of pigment (hemosiderin) in the joints and formation of focal nodules and follicles. It most commonly occurs in patients between the ages of 20 and 50 years and mainly affects large joints such as the knee and hip joints.
Aim:	Presentation of the clinical picture, laboratory findings and treatment of a patient with PVNS and review of the recent literature regarding this disease.
Methods:	We conducted a recent literature search on the PubMed / MEDLINE website until 12/2019.
Results – Case Report:	A 37-year-old man, with a free personal and family medical history, presented with a six month edema, gradually worsening pain and reduced functionality in the knee joint area. Orthopedic assessment was performed and initially treated it as a case of patellar chondropathy. The X-ray images of the area were normal. The patient then underwent an MRI scan and a biopsy (with a small anterior approach), which was used to diagnose PVNS. He underwent two procedures for the surgical resection of the lesion in a time period of two months due to residual disease. He then underwent postoperative radiotherapy (38 Gy, in 19 sessions, with a daily dose of 2 Gy), four weeks after the second surgery, due to diffuse PVNS.
Conclusions:	Adjuvant postoperative radiotherapy can improve the percentage of local control in case of diffuse PVNS and reduce the chance of recurrence.

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DUCTAL CARCINOMA OF THE BREAST: AN INCIDENTAL FINDING IN FIBROADENOMA. AN INTERESTING CASE

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Introduction: Fibroadenoma is the most frequent benign tumor of the female breast, which appears often in adolescents and young women, and the peak age of incidence is the 2nd – 3rd decade of life. It is a biphasic, histologically, neoplasm, consisting of an epithelial glandular portion and the specialized stroma of the terminal ductal lobular unit (T.D.L.U). It can be single or multiple and bilateral. Its size is generally smaller than 3 cm, although it may be large sized. On ultrasound imaging, it appears as a hypo- or isoechoic ovular mass with regular margins.

Aim: The presentation of a rare case of ductal carcinoma of the breast as an incidental finding during the cytological examination of a fibroadenoma.

Methods: A female patient 46 years old was referred to our laboratory for ultrasound-guided fine needle aspiration (FNA) of a compact tumor in the right breast below and in the external region of the nipple, 6 millimeters in diameter.

Results: The cytological examination of the smears of the FNA specimen revealed a lot of cellular aggregations, with nuclear crowding and overlapping. In many sites architectural distortion was observed with loss of cellular cohesion and cellular spreading. The cells had eccentric nuclei and nucleoli, whereas they were positive for p53. Also, a lot of cellular aggregations were revealed, characteristic for fibroadenoma. These findings were compatible with ductal adenocarcinoma of the breast with coexisting fibroadenoma.

Conclusions: The development of carcinoma in a fibroadenoma an extremely rare incident. The frequency in retrospective studies is considered 0,002-0,0125%. Carcinomas can develop inside a benign lesion or they may coexist independently. Generally, fibroadenoma is not considered a risk factor for development of cancer, however the existence of characteristics which classify it as complex, such as sclerotic adenosis, calcifications and the papillary apocrine metaplasia, increase this risk. Also, the presence of hyperplastic lesions in the surrounding parenchyma increase more the risk. The correct cytological assessment is necessary also in lesions that do not raise clinical and imaging suspicions for malignancy.

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WARTHIN TUMOR: A CASE REPORT

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Introduction: Cystadenolymphoma (Warthin Tumor) is a benign tumor of the salivary glands. It is the second most frequent tumor after pleiomorphic adenoma, and it concerns 10% of all tumors of the parotid gland. The majority of this tumors is found in the parotid and occasionally in the buccal cavity, larynx, and the cervical lymph nodes. It is more frequent in male smokers, aged 40 years and over. Histologically is characterized by a double layer of epithelial cells in dense lymphoid stroma with frequent lymph follicles. Malignant transformation to lymphoma, Merkel cell carcinoma, adenocarcinoma, mucoepidermoid carcinoma, squamous cell carcinoma and others is rare. The preoperative diagnosis is based mainly in Fine Needle Aspiration and the Cytological Examination.

Aim: The presentation of an interesting case of cystadenolymphoma which cytologically imitated squamous cell carcinoma.

Methods: A male patient 54 years old with painless enlargement at the right parotid region. Clinically and radiologically it was considered as possible malignancy. Patient underwent ultrasound-guided fine needle aspiration.

Results: The cytological examination of the smears revealed sparse or small aggregations of oncocytes with granular cytoplasm, hyperchromatic nuclei, occasional nucleoli, and a lot of spindle-shaped squamous atypical cells. In the substrate, a lot of histiocytes were found and a lot of inflammatory cells, amorphous substance, and necrotic elements. These findings corresponded to cystadenolymphoma with features suggesting squamous metaplasia, however the histological examination, which was considered necessary, confirmed the cytological findings.

Conclusions: Cystadenolymphoma is a frequent benign tumor of the parotid with extremely good prognosis and infrequent recurrences (2%). In rare cases it could be a diagnostic trap even for the experienced cytologist. The main malignancies with which should be distinguished are mucoepidermoid carcinoma, squamous cell carcinoma, mainly in cases with extended mucinous and squamous metaplasia. The possibility of false positive results should be taken in consideration by the clinicians, especially in cases where the clinical and the other findings do not suggest malignancy.

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THE ROLE OF CHEMOTHERAPY IN WEIGHT GAIN IN WOMEN WITH BREAST CANCER

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Introduction: Women who receive chemotherapy for treatment of the breast cancer, have a tendency to gain weight. About 50 to 90% of women had gain weight and 20% of them had gain a total weight of more than 10 kilos.

Aim: The aim of this review is to investigate the association between chemotherapy and weight gain in women receiving chemotherapy.

Methods: A literature review was conducted using the electronic databases PubMed and Google scholar. The following key words were entered: "weight gain", "chemotherapy", "breast cancer" and "cancer patients" and a combination thereof. Exclusion criteria of articles were the language, except English and the type of cancer that exclusively concerned women with breast cancer. About 30 articles were found on the subject and 15 of them were included. The review was conducted in the last 20 years

Results: Factors that contribute to weight gain during chemotherapy are the intake of large amounts of food associated with stress, reduced physical activity and also the modification of basic metabolic rate. Additionally, women in premenopausal period and use of corticosteroids in chemotherapy protocols have been identified as risk factors for weight gain. Weight gain is predisposed to chronic diseases such as high blood pressure, diabetes and osteoarthritis, which negatively affect quality of life and possibly the survival of these patients.

Conclusions: Weight gain in women with breast cancer receiving chemotherapy is a common side effect of treatment. Healthcare professionals need to inform patients about this possibility in order to be properly prepared and follow a diet that will allow them to maintain a normal weight throughout the treatment in order to avoid the occurrence of chronic diseases.

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POSTOPERATIVE RUPTURE OF PANCREATIC ANASTOMOSIS AFTER PANCREATICODUODENECTOMY (WHIPPLE) IN PANCREATIC ADENOCARCINOMA AND NURSING CARE: CASE STUDY

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Introduction: Pancreatic adenocarcinoma is the most common type of pancreatic cancer and is a leading cause of death worldwide. It is a very aggressive type of cancer with a life expectancy of five years. Whipple surgery, which is used to treat pancreatic adenocarcinoma and is one of the most complex oncological surgeries, involves the removal of the pancreas head, lymph node clearance of the area as well as pancreato static, cholepeptic and gastronomic anastomosis. Rupture of pancreato static anastomosis with pancreatic fluid leakage is the most common postoperative complication.

Aim: The aim of the study is to describe an incident involving the rupture of pancreato static anastomosis after Whipple surgery.

Methods: This is a case study of a 63-year-old woman who underwent surgery to remove a pancreatic adenocarcinoma in a large hospital in northern Greece.

Results: A 63-year-old female patient with pancreatic head adenocarcinoma arrived in May 2019 for surgery. The patient underwent pancreatodecadactylectomy with lymph node dissection and the development of gastronomic, pancreato static and biliary-fasting anastomosis. For the first 24 hours the patient was transferred to the clinic, while on the second postoperative day, the patient had a good postoperative course. On the tenth postoperative day, she presented with rupture of pancreatic anastomosis with pancreatic fistula formation, while on the twelfth day she presented hemodynamic instability. The rupture was treated with more adequate drainage and administration of somatostatin, while she also underwent a computed tomography scan. Nursing care consisted of evaluating the functioning of the drainage system, monitoring the patient's body temperature, replenishing oxygen in the blood and monitoring blood glucose levels regularly. In order to prevent a more serious hemodynamic complication, the nurse monitored the patient's vital signs and urination every three hours.

Conclusions: Rupture of pancreatic anastomosis is a life-threatening complication. When it occurs, appropriate nursing care is required to treat it adequately.

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CARCINOMA OF UNKNOWN PRIMARY SITE INITIALLY PRESENTING WITH CARDIAC TAMPONADE: A RARE CASE

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Introduction: Carcinomas of unknown primary site are a heterogenous group of neoplasms with poor prognosis. Their frequency ranges from 2% to 4 % of all patients with cancer. They may present as multiple sites in the liver, as lymphadenopathy of mediastinum, retroperitoneum, head, axilla, or inguinal region, as peritoneal carcinomatosis and also as multiple nodular sites in the pulmonary parenchyma or as metastatic sites in the bones or the brain. Malignant effusions in serous cavities may be the first manifestation of a malignancy. However, cardiac tamponade resulting from malignant pericardial effusion is rarely the first presentation of an undiagnosed malignancy.

Aim: The presentation of a case of adenocarcinoma of unknown primary site which manifested with cardiac tamponade.

Methods: A male patient, 40 years old, with free personal anamnesis, came with productive cough for the last five days, retrosternal pain and fever. The clinical examination revealed tachycardia, tachypnea, and hypotension. Electrocardiogram, cardiac ultrasound, and further imaging showed a large pericardial effusion and cardiac tamponade. Also, CT scan revealed mediastinal lymphadenopathy. Patient underwent aspiration of pericardial cavity and we received the liquid for cytological examination.

Results: The cytological examination of the smears from the aspiration specimen (pericardial fluid) revealed a lot of malignant cells in papillary aggregations with nuclear overlapping, hyperchromasia, multiple nucleoli and vacuolated cytoplasm. The immunophenotype was MOC-31 (+), CK7 (+), CK20 (+), WT-1 (-). These findings were compatible with metastatic adenocarcinoma. Despite the detailed clinical and laboratory investigations and the histological – immunohistochemical investigation of lymph nodes, the determination of the primary site was not possible.

Conclusions: A malignant pericardial effusion is observed sometimes during the course of diagnosed malignant neoplasms. Rarely, cardiac tamponade is the first presentation of a malignancy, however it should be included in the differential diagnosis of this critical condition. The primary site is more often found in the lung, the breast, or the lymphatic system. In our case, the primary site was not found. Patient receives chemotherapy neoplasms of unknown primary site an after a month he presents an improved clinical condition.

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RECURRENT RECTAL CANCER IN THE SMALL BOWEL

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Introduction: Colorectal cancer (CRC) is a major cause of morbidity and mortality worldwide and despite improvements in surgical techniques, chemotherapy, and radiotherapy, the incidence of local recurrence still ranges between 4% -8%, with distant recurrences predominating (1,2)

Aim: The purpose of this article is to present a clinical case of rectal cancer, with rare recurrence (small intestine) and how it was treated.

Case report: A 65-year-old patient was diagnosed with grade II rectal adenocarcinoma and received neoadjuvant chemotherapy with concurrent radiotherapy and then underwent low anterior resection and afterwards he received adjuvant chemotherapy. Immunohistochemical study revealed intestinal adenocarcinoma with CK7 (-), CD20 (+), CDX2 (+) and DPC4 (+).

Two years later, as part of the follow-up, he underwent an abdominal CT scan and a thickening of the second part of duodenum was revealed. He underwent a gastroscopy and biopsy of the suspicious site, and an intestinal adenocarcinoma with a similar immunophenotype to rectal cancer, namely CK7 (-), CD20 (+), CDX2 (+) and DPC4 (+). An integrated positron emission tomography (PET)/CT scan was performed, that showed increased metabolic activity [standardized uptake values (SUV): 10,3] only in the second part of the duodenum and a right hemicolectomy was performed.

Conclusions: The most common sites of metastatic rectal cancer are the liver, lungs, peritoneum, retroperitoneally, and lymph nodes (2). Small intestine tumors account for only 2% of gastrointestinal tumors and mainly involve primary tumors, such as adenocarcinomas, GIST, carcinoids, and lymphomas (3). Metastatic disease in the small intestine is rare and comes mainly from melanoma and breast or lung cancer (4).

The recurrence of rectal cancer in the small intestine is possible, but a detailed pathological and immunohistochemical study is required to differentiate primary small intestine cancer from metastatic rectal cancer and future studies are required to address what kind of surgery and chemotherapy is necessary.

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PANCREATIC CARCINOSARCOMA: A RARE CASE

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Introduction: Carcinosarcoma is an unusual type of malignant neoplasm of the pancreas which is characterized by a biphasic morphology, with coexistence of epithelial and sarcomatous components. Each of these components has distinctive morphological and immunohistochemical characteristics. They are usually arising in uterus. Their localization in pancreas is extremely rare (7% of the non-neuroendocrine malignant neoplasms), with few cases reported in international bibliography (less than 20). Their histogenesis remains still unclear and the small number of the studied cases does not allow the determination of an appropriate treatment. They are extremely aggressive neoplasms with poor prognosis (mean survival time 6 months). They mostly affect women in the 7th decade of life.

Aim: The presentation of a rare case of pancreatic carcinosarcoma in a male patient 59 years old

Methods: A male patient 59 years old came with abdominal pain during the last month. By his medical history, an episode of acute pancreatitis was reported one year before. Ultrasound imaging revealed the presence of a cystic and partially compact lesion in the body of pancreas, approximately 6 cm in diameter. Patient underwent ultrasound-guided fine needle aspiration (EUS-FNA)

Results: The cytological examination of the smears revealed a lot of flat and three-dimensional groups of cells with nuclear crowding / overlapping, well-sized and frequently multiform nuclei with thickened nuclear membrane and often visible nucleoli. Also, a lot of aggregations of spindle-shaped cells were observed, with severe atypia and polymorphism, focally with storiform pattern. The substrate was inflammatory, focally with presence of myxomatous substance and frequently necrotic. The above findings were compatible with undifferentiated carcinoma, of carcinosarcoma type. Patient underwent peripheral pancreatectomy and the diagnosis was confirmed histologically.

Conclusions: Pancreatic carcinosarcoma is an extremely aggressive neoplasm and its preoperative diagnosis is a challenge even for the experienced cytologists. Although rare, it should be included in the differential diagnosis of pancreatic tumors, especially of the tumors with cystic degeneration. EUS-FNA technique is a reliable method of diagnostic approach.

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MUCINOUS CARCINOMA OF THE BREAST: A RARE CASE

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Introduction: Mucinous carcinoma (colloid, gelatinous) of the breast is a rare type of a well differentiated infiltrative carcinoma, representing 0,5 – 3% of breast carcinomas in its pure form. It is met more frequently in post-menopausal women (mean age 71 years). Histologically, it is characterized by the presence of nests of cells in lakes of mucin, separated by thin fibrous septae including capillary blood vessels. By definition, the mucin lakes represent 50% of the tumor. It is distinguished in the pure mucinous type (pure when the mucinous characteristics concern more than 90% of its total extent) and the mixed type, which has worse prognosis. Cellular atypia is generally low.

Aim: The presentation of a rare case of mucinous carcinoma of the breast, which was diagnosed cytologically.

Methods: A woman, 79 years old, with an incidental finding in chest CT scan concerning a lesion in the left breast, which ultrasonographically was considered suspicious for malignancy. She was referred for ultrasound-guided fine needle aspiration (FNA) of the lesion. Lymphadenopathy was not observed.

Results: The cytological examination of the smears revealed loose aggregations of tumor cells, architectural distortion, and sometime single cells, with moderate polymorphism, eccentric nuclei, irregular chromatin network and occasionally visible nucleoli. The substrate was inflammatory, focally necrotic, with stromal cells and vessels with shapeless mucinous substance. The aforementioned cytolmorphological findings were compatible with mucinous carcinoma of the breast of pure type.

Conclusions: Mucinous carcinoma of the breast is an interesting type of carcinoma, on the one hand because of its rarity and on the other hand because of its favorable prognosis. Lymph node metastasis is rare (2-4%). Ten-year survival ranges between 80% and 100%. Thus, its early diagnosis and its distinction from a lot of other benign and malignant lesions is of great importance. The similarities with lesions such as mucocele and myxoid adenoma could be a diagnostic trap. FNAC is a reliable technique for pre-operative diagnosis.

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INTRA-ABDOMINAL EXTRAGASTROINTENSTINAL STROMAL TUMOR (EGIST): A RARE CASE

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Introduction: Gastrointestinal Stromal Tumors (GISTs) are the most frequent mesenchymal tumors of the gastrointestinal tract. They are rare neoplasms and they represent less than 1% of all primary neoplasms of the gastrointestinal tract. They appear more often in the 5^{th} – 6^{th} decade of life. They are characterized by the mutation of KIT proto-oncogene (75%) or PDGFR-α (10%). They can develop throughout the gastrointestinal tract, however they are localized more often in the stomach (60-70%) and small intestine (25-35%), whereas they may appear in the colon, rectum, esophagus, and appendix. Rarely they primarily develop in the intra-abdominal tissues outside the gastrointestinal tract and then they are characterized as EGISTs (5% of the cases in the omentum, mesentery and retroperitoneum).

Aim: The presentation of a rare case of EGIST, which was diagnosed preoperatively with FNAC-CT.

Methods: A male patient, 71 years old, came with abdominal pain and abdominal distention during the last weeks. Imaging (CT scan) revealed the presence of an intra-abdominal mass, approximately 16 cm in maximum diameter, which was pushing away the surrounding structures. CT-guided fine needle aspiration was performed (FNA-CT).

Results: The cytological examination of the smears revealed single neoplastic cells or in loose aggregations, with nuclear overlapping, elongated / wavy nuclei, and fibrous cytoplasm, sometimes with cytoplasm of fibrous texture and cytoplasmic projections (snouts). The substrate was focally fibrous or moderately inflammatory, with cellular debris. The above findings in correlation with radiological findings were compatible with extragastrointestinal stromal tumor (EGIST). Resection was performed and the diagnosis was confirmed histologically by the surgical specimen.

Conclusions: EGISTs are rare neoplasms. They often present with non-specific symptoms and their preoperative diagnosis is sometimes difficult. They should be distinguished from leiomyomata, leiomyosarcomas, schwannomas, solitary fibrous tumors and also carcinomas, neuroendocrine tumors, and melanomas. FNAC in combination with immunocytochemistry is a valuable tool of preoperative diagnosis. Prognosis depends of grading (size of the tumor, number of mitoses), as this is determined in the surgical specimen.

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SYNCHRONOUS PRIMARY ADENOCARCINOMA OF THE PANCREAS AND SQUAMOUS CELL CARCINOMA OF THE LUNG: CASE REPORT

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Introduction: Multiple primary cancers are usually defined as primary malignant tumors in different sites and with different histological origins in one person. The incidence of multiple primary malignancies seems to be increasing because of the increasing overall life expectancy, better cancer therapies and more sensitive modalities for detection. The reported frequency of multiple synchronous primary tumors is 1–3%. The frequency of pancreatic cancer in association with cancer of other organs is estimated to range from 1% to 20%. The presence of synchronous lung and pancreatic cancers is extremely rare . Smoking, genetic factors and chronic inflammation are supposed to be risk factors.

Aim: The presentation of an interesting case of a 60-yaer-old male with synchronous primary pancreatic adenocarcinoma and squamous carcinoma of the lung.

Methods: A 60-year-old male, who was recently diagnosed with squamous carcinoma of the lung, was referred to the Oncology Department for therapy. PET/CT revealed a mass in the tail of pancreas. ERCP was performed and samples were taken.

Results: Cytopathology demonstrated multiple groups with disordered sheets of cells displaying a drunken honeycomb pattern, grooved nuclei and prominent nucleoli. These findings were compatible with pancreatic adenocarcinoma. The patient takes chemotherapy and shows no signs of regression.

Conclusions: The diagnosis of multiple primary in a patient, though rare, is of great importance and poses crucial dilemmas about the therapy. The early recognition and treatment is important as there exists a significant survival difference in patients who have synchronous primaries as opposed to those with metastatic pancreatic adenocarcinoma.

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Abstract: A text of no more than 250 words, consisting of Background, Patients & Methods, Results and Conclusions. The primary goal of the abstract should be to make the general significance and conceptual advance of the work clearly accessible to a broad readership.

References should not be cited in the abstract.

Key Words: 5-10, for indexing purposes.

Introduction: Provides a context or background for the study (that is, the nature of the problem and its significance) and states the specific purpose or research objective of, or hypothesis tested by, the study or observation.

Patients & Methods: This section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section.

Results: This section presents results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Authors should avoid repeating all the data in the tables or illustrations in the text but should emphasize or summarize only the most important observations. Extra or supplementary materials and technical detail can be placed in an appendix, where they will be accessible but will not interrupt the flow of the text.

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The concluding paragraph should provide the reader with an idea of how the field may develop or future problems to be overcome, but should not summarize the article. To ensure that a review is likely to be accessible to as many readers as possible, it may be useful to ask a colleague from another discipline to read the review before submitting it.

Please include the following:

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3. Others (Letters to the Editors, Clinical Images etc.)

Correspondence

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Authors' names and institutional affiliations.

The name of the department(s) and institution(s) to which the work should be attributed.

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The contact details for authors and the name, address, email, telephone and fax numbers of the corresponding author, who should also clearly indicate whether this e-mail address may be published. 5-10 key words (for indexing purposes).
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Το **LYNPARZA** είναι ο **ΠΡΩΤΟΣ PARPi**[1,2] με ένδειξη ως μονοθεραπεία για τη θεραπεία συντήρησης ενηλίκων ασθενών με προχωρημένο (σταδίου III και IV κατά FIGO (Διεθνής Ομοσπονδία Γυναικολογίας και Μαιευτικής)) υψηλού βαθμού κακοήθειας επιθηλιακό καρκίνο των ωοθηκών, των ωαγωγών ή πρωτοπαθή καρκίνο του περιτοναίου, που φέρουν μεταλλαγμένα γονίδια BRCA1/2 (γεννητικών και/ή σωματικών κυττάρων) και οι οποίες εμφανίζουν ανταπόκριση (πλήρη ή μερική) έπειτα από την ολοκλήρωση της χημειοθεραπείας πρώτης γραμμής με βάση την πλατίνα.[1,2]

- Αποτελεσματική θεραπεία με το **60%** των ασθενών **χωρίς εξέλιξη της νόσου στα 3 χρόνια** έναντι 27% στο σκέλος ελέγχου, (HR = 0.30; 95% CI: 0.23-0.41; *P*<0.0001)[1,2]
- **70%** μείωση του κινδύνου εξέλιξης της νόσου ή θανάτου[1,2]

Βιβλιογραφία: 1. Lynparza [Summary of product characteristics]. Bedfordshire, UK: AstraZeneca UK Ltd; 2019; **2.** Moore K, Colombo N, Scambia G, et al. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med. 2018;379(26):2495-2505.

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1. ΟΝΟΜΑΣΙΑ ΤΟΥ ΦΑΡΜΑΚΕΥΤΙΚΟΥ ΠΡΟΪΟΝΤΟΣ: Lynparza 100 mg επικαλυμμένα με λεπτό υμένιο δισκία. Lynparza 150 mg επικαλυμμένα με λεπτό υμένιο δισκία. **2. ΠΟΙΟΤΙΚΗ ΚΑΙ ΠΟΣΟΤΙΚΗ ΣΥΝΘΕΣΗ** Lynparza 100 mg επικαλυμμένα με λεπτό υμένιο δισκίο Κάθε επικαλυμμένο με λεπτό υμένιο δισκίο περιέχει 100 mg ολαπαρίμπης. Lynparza 150 mg επικαλυμμένα με λεπτό υμένιο δισκίο Κάθε επικαλυμμένο με λεπτό υμένιο δισκίο περιέχει 150 mg ολαπαρίμπης. Έκδοση με γνωστή δράση: Αυτό το φαρμακευτικό προϊόν περιέχει 0,24 mg νατρίου ανά δισκίο 100 mg και 0,35 mg νατρίου ανά δισκίο 150 mg, δηλαδή είναι ουσιαστικά «ελεύθερο νατρίου». **4. ΚΛΙΝΙΚΕΣ ΠΛΗΡΟΦΟΡΙΕΣ 4.1 Θεραπευτικές ενδείξεις:** Καρκίνος των ωοθηκών Το Lynparza ενδείκνυται ως μονοθεραπεία για τη: • Θεραπεία συντήρησης ενηλίκων ασθενών με προκαιμφίβολο (σταδίου III και IV κατά FIGO (Διεθνής Ομοσπονδία Γυναικολογίας και Μαιευτικής) ψηλού βαθμού καρκίνο των ωοθηκών, των ωογόνων ή πρωτοπαθή καρκίνο του περιτοναίου, που φέρουν μεταλλαγμένα γονίδια *BRCA1/2* (γενετικών και/ή σωματικών κυττάρων) και οι οποίες εμφανίζουν ανταπόκριση (πλήρη ή μερική) έπειτα από την ολοκλήρωση της πλατινοθεραπείας πρώτης γραμμής με βάση την πλατίνα. • Θεραπεία συντήρησης ενηλίκων ασθενών με ευαίσθητο στην πλατίνα υποτροπιάζοντα ψηλού βαθμού καρκίνθηκε επιθηλιακό καρκίνο των ωοθηκών, των ωογόνων ή πρωτοπαθή καρκίνο του περιτοναίου, οι οποίοι εμφανίζουν ανταπόκριση (πλήρη ή μερική) σε πλατινοθεραπεία με βάση την πλατίνα. Καρκίνος του μαστού Το Lynparza ενδείκνυται ως μονοθεραπεία για τη θεραπεία ενηλίκων ασθενών με τοπικά προχωρημένο ή μεταστατικό καρκίνο του μαστού και γερμινικές μεταλλάξεις των *BRCA1/2*, και των οποίων ο όγκος είναι αρνητικός για τον υποδοχέα τύπου 2 του ανθρώπινου επιδερμικού αυξητικού παράγοντα (HER 2). Οι ασθενείς θα πρέπει να έχουν προηγουμένως υποβληθεί σε θεραπεία με ανθρακυκλίνη και μία ταξάνη είτε για επαναλαμβάνη είτε για μεταστατική νόσο εκτός εάν οι ασθενείς δεν ήταν κατάλληλοι για αυτές τις θεραπείες (βλ. παράγραφο 5.1). Οι ασθενείς με θετικά στους ορμονικούς υποδοχείς (HR) καρκίνο του μαστού πρέπει επίσης να παρουσιάζουν εξέλιξη κατά τη διάρκεια ή μετά από προηγούμενη ενδοκρινική θεραπεία ή να θεωρούνται ακατάλληλοι για ενδοκρινική θεραπεία. **4.3 Αντενδείξεις:** Υπερευαισθησία στη δραστική ουσία ή σε κάποιο από τα έκδοχα που αναφέρονται στην παράγραφο 6.1. Θηλασμός κατά τη διάρκεια της θεραπείας και για διάστημα 1 μηνός μετά την τελευταία δόση. **4.4 Ειδικές προειδοποιήσεις και προφυλάξεις κατά τη χρήση** Αιματολογική τοξικότητα Σε ασθενείς που λαμβάνουν θεραπεία με Lynparza έχει αναφερθεί αιματολογική τοξικότητα, περιλαμβανομένων κλινικών διαγνώσεων και/ή εργαστηριακών ευρημάτων γενικά ήπιας ή μέτριας (βαθμού 1 ή 2 κατά CTCAE) αναιμίας, ουδετεροπενίας, θρομβοπενίας και λεμφοπενίας. Οι ασθενείς δεν πρέπει να ξεκινούν θεραπεία με το Lynparza μέχρις ότου ανακάμψουν από την αιματολογική τοξικότητα που έχει προκληθεί από προηγούμενη αντικαρκινική θεραπεία (τα επίπεδα αιμοσφαιρίνης, αιμοπεταλίων και ουδετερόφιλων πρέπει να είναι ≤ βαθμού 1 κατά CTCAE). Συνιστάται η διενέργεια εξετάσεων κατά την έναρξη της θεραπείας και ακολούθως παρακολούθηση των γενικών εξετάσεων αίματος με μηνιαία βάση για τους πρώτους 12 μήνες θεραπείας και εν συνεχεία κατά περιοδική διαστήματα για την εμφάνιση κλινικά σημαντικών μεταβολών οποιασδήποτε παραμέτρου κατά τη διάρκεια της θεραπείας (βλ. παράγραφο 4.8). Εάν κάποιος ασθενής αναπτύξει αιματολογική τοξικότητα βαριάς μορφής ή εξάρτηση από μεταγγίσεις αίματος, η θεραπεία με το Lynparza πρέπει να διακόπτεται και να ξεκινούν κατάλληλες αιματολογικές εξετάσεις. Εάν οι αιματολογικές παράμετροι παραμείνουν κλινικά μη φυσιολογικές μετά από τη διακοπή της δόσης του Lynparza για 4 εβδομάδες, συνιστάται εξέταση του μυελού των οστών και/ή κυτογενετική ανάλυση αίματος. Μυελοδυσπλαστικό σύνδρομο/Οξεία μυελογενής λευχαιμία Η συνολική επίπτωση μυελοδυσπλαστικού συνδρόμου/οξείας μυελογενούς λευχαιμίας (ΜΔΣ/ΟΜΛ) σε ασθενείς που έλαβαν θεραπεία στο πλαίσιο κλινικών μελετών με μονοθεραπεία Lynparza, συμπεριλαμβανομένης της παρακολούθησης μακροχρόνιας επίθεσης, ήταν <1,5% και η πλειοψηφία των συμβάντων είχαν θανατηφόρο έκβαση. Η διάρκεια της θεραπείας με την ολαπαρίμπη σε ασθενείς που ανέπτυξαν ΜΔΣ/ΟΜΛ κυμαινόταν από < 6 μήνες έως > 2 χρόνια - δεδομένα με μεγαλύτερες διάρκειες έκθεσης είναι περιορισμένα. Όλοι οι ασθενείς είχαν δυνητικά επιβαρυντικούς παράγοντες για την ανάπτυξη ΜΔΣ/ΟΜΛ, έκοντας λάβει προηγούμενη χημειοθεραπεία με παράγοντες πλατίνας. Αρκετοί είχαν λάβει επιπλέον άλλους παράγοντες που προκαλούν βλάβη στο DNA και είχαν υποβληθεί σε ακτινοθεραπεία. Η πλειοψηφία των αναφορών ήταν μεταξύ γενιδίων 1 ή 2 προδιάθεσης καρκίνου του μαστού (gBRCA1/2). Η συνολική εμφάνιση περιπτώσεων ΜΔΣ/ΟΜΛ στον παρόμοιο μεταξύ των ασθενών με γερμινικές μεταλλάξεις gBRCA1m και gBRCA2m (1,7% και 1,4%, αντίστοιχα). Ορισμένοι από τους ασθενείς είχαν ιστορικό προηγούμενου καρκίνου ή δυσπλασίας του μυελού των οστών. Εάν επιβεβαιωθεί η παρουσία ΜΔΣ και/ή ΟΜΛ κατά τη διάρκεια της θεραπείας με το Lynparza, συνιστάται η διακοπή του Lynparza και η κατήγηση κατάλληλης θεραπείας στον ασθενή. Πνευμονίτιδα Πνευμονίτιδα, συμπεριλαμβανομένων των συμβάντων με θανατηφόρο έκβαση, έχει αναφερθεί σε ποσοστά <1,0% των ασθενών που έλαβαν Lynparza σε κλινικές μελέτες, συμπεριλαμβανομένων των συμβάντων με θανατηφόρο έκβαση. Οι αναφορές πνευμονίτιδας δεν είχαν σταθερή κλινική εικόνα και περιλήφθηκαν από μια σειρά προδιαθεσικών παραγόντων (καρκίνου και/ή μετάστασεων στους πνεύμονες, υπαρξιακής πνευμονικής νόσου, ιστορικού καπνίσματος, και/ή προηγούμενης χημειοθεραπείας και ακτινοθεραπείας). Εάν οι ασθενείς εμφανίσουν νεοσχηματίζομενα ή επιδεινούμενα αναπνευστικά συμπτώματα, όπως δυσπνοια, βήχα και πυρετό, ή εάν παρατηρηθεί ένα παθολογικό θωρακικό ακτινολογικό εύρημα, η θεραπεία με το Lynparza πρέπει να διακόπτεται και να ξεκινά άμεσα η διενέργεια εξετάσεων. Εάν επιβεβαιωθεί πνευμονίτιδα, η θεραπεία με το Lynparza πρέπει να διακόπτεται και οι ασθενείς να αντιμετωπίζονται κατάλληλα. Εμβρυική τοξικότητα Με βάση τον μηχανισμό δράσης (αναστολή της PARP), το Lynparza θα μπορούσε να προκαλέσει βλάβη στο έμβρυο όταν χορηγείται σε μια έγκυο γυναίκα. Οι μη κλινικές μελέτες σε επίμυες έχουν δείξει ότι η ολαπαρίμπη προκαλεί ανεπιθύμητες ενέργειες στην εμβρυική επιβίωση και επιφέρει μειζόνες δυσπλασίες του εμβρύου σε εκθέσεις χαμηλότερες από εκείνες που αναμένονται με τη συνιστώμενη δόση των 300 mg δις ημερησίως για τον άνθρωπο. Εγκυμοσύνη/αντισύλληψη Το Lynparza δεν πρέπει να χρησιμοποιείται κατά τη διάρκεια της εγκυμοσύνης. Οι γυναίκες σε αναπαραγωγική ηλικία πρέπει να χρησιμοποιούν δύο μορφές αξιόπιστης αντισύλληψης πριν την έναρξη της θεραπείας με Lynparza, κατά τη διάρκεια της θεραπείας και για διάστημα 1 μηνός μετά τη λήψη της τελευταίας δόσης του Lynparza (βλ. παράγραφο 4.6). Συνιστώνται δύο συμπληρωματικές αποτελεσματικές και συμπληρωματικές μορφές αντισύλληψης. Οι άρρενες ασθενείς και οι θήλεις σύντροφοί τους σε αναπαραγωγική ηλικία πρέπει να χρησιμοποιούν αξιόπιστη αντισύλληψη κατά τη διάρκεια της θεραπείας και για διάστημα 3 μηνών μετά τη λήψη της τελευταίας δόσης του Lynparza (βλ. παράγραφο 4.6). Αλληλεπιδράσεις Δεν συνιστάται η συγχορήγηση του Lynparza με ισχυρά ή μέτρια αναστολέα του CYP3A (βλ. παράγραφο 4.5). Εάν πρέπει να συγχορηγηθεί ισχυρός ή μέτριος αναστολέας του CYP3A, η δόση του Lynparza πρέπει να μειωθεί (βλ. παραγράφους 4.2 και 4.5). Δεν συνιστάται η συγχορήγηση του Lynparza με ισχυρούς ή μέτριους επαγωγείς του CYP3A. Σε περίπτωση που ένας ασθενής ο οποίος λαμβάνει ήδη Lynparza αποφασίσει θεραπεία με ισχυρό ή μέτριο επαγωγέα του CYP3A, ο συνταγογράφων θα πρέπει να γνωρίζει ότι η αποτελεσματικότητα του Lynparza μπορεί να μειωθεί σημαντικά (βλ. παράγραφο 4.5). **4.8 Ανεπιθύμητες ενέργειες** Περίληψη του προφίλ ασφαλείας Η μονοθεραπεία Lynparza έχει συσχετισθεί με ανεπιθύμητες ενέργειες γενικά ήπιας ή μέτριας βαρύτητας (βαθμού 1 ή 2 κατά CTCAE) που δεν απαιτούν σε γενικές γραμμές διακοπή της θεραπείας. Οι συνήθεσο παρατηρούμενες ανεπιθύμητες ενέργειες στις κλινικές μελέτες ασθενών που έλαβαν μονοθεραπεία με Lynparza (≥10%) ήταν ναυτία, έμετος, διάρροια, δυσπεψία, κόπωση, κεφαλαλγία, δυσγευσία, μειωμένη όρεξη, ζάλη όλγος άνω κοιλιακής κώρας βήχας, δυσπνοια, αναιμία, ουδετεροπενία, θρομβοπενία και λευκοπενία. Κατάλογος εμφάνισης των ανεπιθύμητων ενεργειών υπό μορφή πίνακα: Το προφίλ ασφαλείας βασίζεται σε συγκεντρωτικά στοιχεία από 1.826 ασθενείς με συμπαγείς όγκους που έλαβαν μονοθεραπεία με Lynparza σε κλινικές μελέτες στη συνιστώμενη δόση. Οι ακόλουθες ανεπιθύμητες ενέργειες έχουν παρατηρηθεί σε κλινικές μελέτες με ασθενείς που έλαβαν μονοθεραπεία με Lynparza, όπου η έκθεση των ασθενών είναι γνωστή. Οι ανεπιθύμητες ενέργειες του φαρμάκου καταγράφονται ανά Κατηγορία Οργανικό Σύστημα (SOC) από MedDRA και ακολούθως ανά προτιμώμενο όρο κατά MedDRA στον Πίνακα 1. Εντός κάθε Κατηγορίας Οργανικού Συστήματος, οι προτιμώμενοι όροι παρουσιάζονται κατά φθίνουσα συνιστότα και ακολούθως κατά φθίνουσα σοβαρότητα. Οι συνιστότες εμφάνισης των ανεπιθύμητων ενεργειών ορίζονται ως: πολύ συχνές (≥1/10), συχνές (≥1/100 έως <1/10), όχι συχνές (≥1/1.000 έως <1/100), σπάνιες (≥1/10.000 έως <1/1.000), πολύ σπάνιες (<1/10.000), μη γνωστές (δεν μπορούν να εκτιμηθούν με βάση τα διαθέσιμα δεδομένα). **Πίνακας 1: Κατάλογος εμφάνισης των ανεπιθύμητων ενεργειών υπό μορφή πίνακα**

Ανεπιθύμητες Ενέργειες		
Κατηγορία/Οργανικό Σύστημα κατά MedDRA	**Συχνότητα Όλων των βαθμών κατά CTCAE**	**Συχνότητα βαθμού 3 και μεγαλύτερου κατά CTCAE**
Διαταραχές του αιμοποιητικού και του λεμφικού συστήματος	**Πολύ συχνές:** Αναιμία[a], Ουδετεροπενία[a], Θρομβοπενία[a], Λευκοπενία[a] **Συχνές:** Λεμφοπενία[a]	**Πολύ συχνές:** Αναιμία[a] **Συχνές:** Ουδετεροπενία[a], Θρομβοπενία[a], Λευκοπενία[a] **Όχι συχνές:** Λεμφοπενία[a]
Διαταραχές του ανοσοποιητικού συστήματος	**Συχνές:** Εξάνθημα[a] **Όχι συχνές:** περευαισθησία[a], Δερματίτιδα[a]	
Διαταραχές του μεταβολισμού και της θρέψης	**Πολύ συχνές:** Μειωμένη όρεξη	**Όχι συχνές:** Μειωμένη όρεξη
Διαταραχές του νευρικού συστήματος	**Πολύ συχνές:** Ζάλη, Κεφαλαλγία, Δυσγευσία	**Όχι συχνές:** Ζάλη, Κεφαλαλγία
Διαταραχές του αναπνευστικού συστήματος, του θώρακα και του μεσοθωράκιου	**Πολύ συχνές:** Βήχας[a], Δύσπνοια[a]	**Συχνές:** Δύσπνοια[a] **Όχι συχνές:** Βήχας[a]
Διαταραχές του γαστρεντερικού	**Πολύ συχνές:** Εμετος, Διάρροια, Ναυτία, Δυσπεψία, Άλγος άνω κοιλιακής κώρας **Συχνές:** Στοματίτιδα[a]	**Συχνές:** Εμετος, Διάρροια, Ναυτία **Όχι συχνές:** Στοματίτιδα[a], Άλγος άνω κοιλιακής κώρας
Γενικές διαταραχές και καταστάσεις της οδού εορήγησης	**Πολύ συχνές:** Κόπωση (περιλαμβανομένης εξασθένισης)	**Συχνές:** Κόπωση (περιλαμβανομένης εξασθένισης)
Παρακλινικές εξετάσεις	**Συχνές:** Αυξημένη κρεατινίνη αίματος **Όχι συχνές:** Αύξηση του μέσου όγκου ερυθρών	**Όχι συχνές:** Αυξημένη κρεατινίνη αίματος

[a] Η αναμία περιλαμβάνει προτιμώμενους όρους αναμίας μακροκυτταρικής αναμίας, ερυθροπενίας, μειωμένου αιματοκρίτη, μειωμένης αιμοσφαιρίνης, νορμόχρωμης αναμίας, νορμόχρωμης νορμοκυτταρικής αναμίας, νορμοκυτταρικής αναμίας και μειωμένου αριθμού ερυθροκυττάρων - Η ουδετεροπενία περιλαμβάνει προτιμώμενους όρους ακοκκιοκυτταραιμίας, εμπυρετης ουδετεροπενίας, μειωμένου αριθμού κοκκιοκυττάρων, κοκκιοκυτταροπενίας, ιδιοπαθούς ουδετεροπενίας, ουδετεροπενίας, ουδετεροπενικής λοίμωξης, ουδετεροπενικής σήψης και μειωμένου αριθμού ουδετερόφιλων - Η θρομβοπενία περιλαμβάνει προτιμώμενους όρους μειωμένου αριθμού αιμοπεταλίων, μειωμένης παραγωγής των αιμοπεταλίων, μειωμένου αιμοπεταλιοκρίτη και θρομβοπενίας - Η λευκοπενία περιλαμβάνει προτιμώμενους όρους λευκοπενίας και μειωμένου αριθμού λευκοκυττάρων - Η λεμφοπενία περιλαμβάνει προτιμώμενους όρους μειωμένου αριθμού Β λεμφοκυττάρων, μειωμένου αριθμού λεμφοκυττάρων, λεμφοπενίας και μειωμένου αριθμού Τ λεμφοκυττάρων - Ο βήχας περιλαμβάνει προτιμώμενους όρους βήχα και παραγωγικού βήχα - Το εξάνθημα περιλαμβάνει προτιμώμενους όρους απορολόδωκού εξανθήματος γενικευμένου ερυθήματος, εξανθήματος ερυθηματώδους, εξανθήματος γενικευμένου, εξανθήματος κνιδώδους, εξανθήματος κνιδοβλατιδώδους, εξανθήματος βλατιδώδους και εξανθήματος κνησμώδους. Η υπερευαισθησία περιλαμβάνει προτιμώμενους όρους υπερευαισθησίας σε φάρμακα και υπερευαισθησίας - Η δερματίτιδα περιλαμβάνει προτιμώμενους όρους δερματίτιδος, δερματίτιδος αλλεργικής και δερματίτιδος απορολόδωκής - Η δύσπνοια περιλαμβάνει προτιμώμενους όρους δύσπνοιας και δύσπνοιας κόπωσης - Η στοματίτιδα περιλαμβάνει προτιμώμενους όρους αφθώδους έλκους, εξέλκωσης του στόματος και στοματίτιδας

Παραγραφή επιλεγμένων ανεπιθύμητων ενεργειών: Αιματολογική τοξικότητα Η αναμία και οι άλλες αιματολογικές τοξικότητες ήταν γενικά κατηλλοί βαθμού (βαθμός 1 ή 2 κατά CTCAE), ωστόσο υπήρχαν αναφορές συμβάντων βαθμού 3 κατά CTCAE και υψηλότερου. Η αναμία ήταν η πιο συνηθισμένη βαθμού ≥3 κατά CTCAE ανεπιθύμητη ενέργεια που αναφέρθηκε σε κλινικές μελέτες. Ο διάμεσος χρόνος της πρώτης εμφάνισης της αναμίας ήταν περίπου 4 εβδομάδες (περίπου 7 εβδομάδες για συμβάντα βαθμού ≥3 κατά CTCAE). Η αναμία αντιμετωπίστηκε με διακοπές δόσεων και μειώσεις δόσεων (βλέπε παράγραφο 4.2) και όπου ενδείκνυται με μεταγγίσεις αίματος. Στις κλινικές μελέτες με το σκεύασμα των δισκίων, η συνολική εμφάνιση της αναμίας ήταν 38,8% (βαθμού ≥3 κατά CTCAE 17,4%) και οι συνότητες των προσωρινών διακοπών, μειώσεων και διακοπών των δόσεων λόγω αναμίας ήταν 15,7%, 10,8% και 1,9%, αντίστοιχα - το 20,9% των ασθενών που έλαβαν θεραπεία με ολαπαρίμπη κρούσκησαν μια ή περισσότερες μεταγγίσεις αίματος. Καταδείκθηκε μία σχέση έκθεσης-αντοπόκρισης μεταξύ της ολαπαρίμπης και των μειώσεων στα επίπεδα αιμοσφαιρίνης. Στις κλινικές μελέτες με Lynparza η συνολότητα εμφάνισης των μεταστάσεων (μείωσης) ≥2 βαθμούς κατά CTCAE από την αρχική τιμή της αιμοσφαιρίνης ήταν 20% των απόλυτων ουδετερόφιλων 20%, των αιμοπεταλίων 5%, των λεμφοκυττάρων 30% και των λευκοκυττάρων 20% (όλα τα κατά προσέγγιση). Η συνότητα εμφάνισης των αυξήσεων στον μέσο όγκο ερυθρών από χαμηλά ή φυσιολογική τιμή κατά την έναρξη σε πάνω από το ULN ήταν περίπου 55%. Τα επίπεδα φόντων για επιστρέφουν στα φυσιολογικά μετά τη διακοπή της θεραπείας και δεν φάνηκε να έχουν απαιτηθεί κλινικές επιπτώσεις. Συνιστάται ο έλεγχος κατά την έναρξη και ακολούθως μηνιαία παρακολούθηση μέσω γενικών εξετάσεων αίματος για τους πρώτους 12 μήνες θεραπείας, καθώς και κατά διαστήματα στη συνέχεια για την παρακολούθηση κλινικά σημαντικών μεταβολών οποιασδήποτε παραμέτρου κατά τη διάρκεια της θεραπείας, που μπορεί να απαιτεί προσωρινή διακοπή της δόσης ή μείωση της δόσης και/ή περαιτέρω θεραπεία (βλ. παραγράφους 4.2 και 4.4). *Άλλα εργαστηριακά ευρήματα:* Στις κλινικές μελέτες με Lynparza η συνολότητα εμφάνισης των μεταστάσεων (αυξήσεις) ≥2 βαθμούς κατά CTCAE από την αρχική τιμή της κρεατινίνης αίματος ήταν περίπου 10%. Δεδομένα από μία διπλά τυφλή ελεγχόμενη με εικονικό φάρμακο μελέτη έδειξαν διάμεση αύξηση έως και 23% από την αρχική τιμή, παραμένοντας σταθερή με τον χρόνο και επιστρέφοντας στην αρχική τιμή μετά τη διακοπή της θεραπείας χωρίς εμφανή κλινικά επακόλουθα. Το 90% των ασθενών είχε τιμές κρεατινίνης βαθμού 0 κατά CTCAE κατά την έναρξη και 10% είχε βαθμού 1 κατά CTCAE κατά την έναρξη. *Γαστρεντερική τοξικότητα:* Ναυτία γενικά αναφέρθηκε πολύ νωρίς με την πρώτη εμφάνιση μέσα στους πρώτους δύο μήνες θεραπείας με Lynparza στην πλειοψηφία των ασθενών. Εμετος αναφέρθηκε νωρίς με την πρώτη εμφάνιση μέσα στους πρώτους δύο μήνες θεραπείας με Lynparza στην πλειοψηφία των ασθενών. Τόσο η ναυτία όσο και ο έμετος αναφέρθηκαν ως διαλείποντα στην πλειοψηφία των ασθενών και μπορούν να αντιμετωπιστούν με προσωρινή διακοπή της δόσης, μείωση της δόσης και/ή αντιεμετική θεραπεία. Αντιεμετική προφυλακτική θεραπεία δεν απαιτείται. Στην πρώτης γραμμής θεραπεία συντήρησης του καρκίνου των ωοθηκών, οι ασθενείς εμφάνισαν συμβάντα ναυτίας (77% υπό ολαπαρίμπη, 38% υπό εικονικό φάρμακο), εμέτου (43% υπό ολαπαρίμπη, 15% υπό εικονικό φάρμακο), διάρροιας (34% υπό ολαπαρίμπη, 25% υπό εικονικό φάρμακο) και δυσπεψίας (17% υπό ολαπαρίμπη, 12% υπό εικονικό φάρμακο). Το συμβάντα ναυτίας οδήγησαν σε διακοπή στο 2,3% των ασθενών υπό θεραπεία με ολαπαρίμπη (βαθμού 2 κατά CTCAE) και στο 0,8% των ασθενών υπό εικονικό φάρμακο (βαθμού 1 κατά CTCAE) - το 0,8% και το 0,4% των ασθενών υπό θεραπεία με ολαπαρίμπη διέκοψε τη θεραπεία λόγω κοιλιακού βαθμού (βαθμού 2 κατά CTCAE) εμέτου και δυσπεψίας, αντίστοιχα. Κανείς από τους ασθενείς υπό θεραπεία με ολαπαρίμπη ή εικονικό φάρμακο δεν διέκοψε τη θεραπεία λόγω διάρροιας. Κανείς από τους ασθενείς υπό θεραπεία με εικονικό φάρμακο δεν διέκοψε τη θεραπεία λόγω εμέτου ή δυσπεψίας. Τα συμβάντα ναυτίας οδήγησαν σε προσωρινή διακοπή της δόσης και σε μειώσεις της δόσης στο 14% και 4%, αντίστοιχα, των ασθενών υπό θεραπεία με ολαπαρίμπη. Τα συμβάντα εμέτου οδήγησαν σε προσωρινή διακοπή στο 10% των ασθενών υπό θεραπεία με ολαπαρίμπη - κανείς από τους ασθενείς υπό θεραπεία με ολαπαρίμπη δεν εμφάνισε κάποιο συμβάν εμέτου που να οδήγησε σε μείωση της δόσης. Παιδιατρικός πληθυσμός: Δεν έχουν πραγματοποιηθεί μελέτες σε παιδιατρικούς ασθενείς. Άλλα ειδικά πληθυσμοί: Τα διαθέσιμα δεδομένα ασφάλειας σε ηλικιωμένα άτομα (ηλικίας ≥ 75 ετών) και ασθενείς που δεν ανήκουν στην Καυκάσια φυλή είναι περιορισμένα. Αναφορά υπολογισμένων ανεπιθύμητων ενεργειών: Η αναφορά υπολογισμένων ανεπιθύμητων ενεργειών μετά από τη κυρήνηση άδειας κυκλοφορίας του φαρμακευτικού προϊόντος είναι σημαντική. Επιτρέπει τη συνεχή παρακολούθηση της σχέσης οφέλους-κινδύνου του φαρμακευτικού προϊόντος. Ζητείται από τους επαγγελματίες υγείας να αναφέρουν οποιεσδήποτε υπολογισμένες ανεπιθύμητες ενέργειες στον Εθνικό Οργανισμό Φαρμάκων. Μεσογείων 284, GR-15562 Χολαργός, Αθήνα. Τηλ: 213 2040380/337. Φαξ: 210 6549585, Ιστοτοπος: http://www.eof.gr. **7. ΚΑΤΟΧΟΣ ΤΗΣ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ:** AstraZeneca AB, SE-151 85 Södertälje, Σουηδία. **8. ΑΡΙΘΜΟΣ(ΟΙ) ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ:** EU/1/14/959/002 EU/1/14/959/003. EU/1/14/959/004, EU/1/14/959/005 **9. ΗΜΕΡΟΜΗΝΙΑ ΠΡΩΤΗΣ ΕΓΚΡΙΣΗΣ/ΑΝΑΝΕΩΣΗΣ ΤΗΣ ΑΔΕΙΑΣ:** Ημερομηνία πρώτης έγκρισης: 16 Δεκεμβρίου 2014. Ημερομηνία τελευταίας ανανέωσης: 01 Οκτωβρίου 2019. **10. ΗΜΕΡΟΜΗΝΙΑ ΑΝΑΘΕΩΡΗΣΗΣ ΤΟΥ ΚΕΙΜΕΝΟΥ:** 01 Οκτωβρίου 2019. Λεπτομερείς πληροφορίες για το παρόν φαρμακευτικό προϊόν είναι διαθέσιμες στον δικτυακό τόπο του Ευρωπαϊκού Οργανισμού Φαρμάκων: http://www.ema.europa.eu. Τιμές Lynparza Χ.Τ.: € 2515,93 / Ν.Τ.: € 2262,11/ Α.Τ.: € 2733,56. Τρόπος διάθεσης: Περιορισμένη ιατρική συνταγή από ειδικό ιατρό και παρακολούθηση κατά τη διάρκεια της αγωγής.

Ανεπιθύμητες Ενέργειες		
Κατηγορία/Οργανικό Σύστημα κατά MedDRA	**Συχνότητα Όλων των βαθμών κατά CTCAE**	**Συχνότητα βαθμού 3 και μεγαλύτερου κατά CTCAE**
Διαταραχές του αιμοποιητικού συστήματος	**Συχνές:** Εξάνθημα[a] **Όχι συχνές:** περευαισθησία[a], Δερματίτιδα[a]	
Διαταραχές του μεταβολισμού και της θρέψης	**Πολύ συχνές:** Μειωμένη όρεξη	**Όχι συχνές:** Μειωμένη όρεξη
Διαταραχές του νευρικού συστήματος	**Πολύ συχνές:** Ζάλη, Κεφαλαλγία, Δυσγευσία	**Όχι συχνές:** Ζάλη, Κεφαλαλγία
Διαταραχές του αναπνευστικού συστήματος, του θώρακα και του μεσοθωράκιου	**Πολύ συχνές:** Βήχας[a], Δύσπνοια[a]	**Συχνές:** Δύσπνοια[a] **Όχι συχνές:** Βήχας[a]
Διαταραχές του γαστρεντερικού	**Πολύ συχνές:** Εμετος, Διάρροια, Ναυτία, Δυσπεψία, Άλγος άνω κοιλιακής κώρας **Συχνές:** Στοματίτιδα[a]	**Συχνές:** Εμετος, Διάρροια, Ναυτία **Όχι συχνές:** Στοματίτιδα[a], Άλγος άνω κοιλιακής κώρας
Γενικές διαταραχές και καταστάσεις της οδού εορήγησης	**Πολύ συχνές:** Κόπωση (περιλαμβανομένης εξασθένισης)	**Συχνές:** Κόπωση (περιλαμβανομένης εξασθένισης)
Παρακλινικές εξετάσεις	**Συχνές:** Αυξημένη κρεατινίνη αίματος **Όχι συχνές:** Αύξηση του μέσου όγκου ερυθρών	**Όχι συχνές:** Αυξημένη κρεατινίνη αίματος

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IBRANCE + Αναστολέας Αρωματάσης[1]
IBRANCE + fulvestrant[1]

1ος στην κατηγορία των CDK4/6 αναστολέων[2]

1η γραμμή θεραπείας και σε επόμενες[3,4]

1 κάψουλα την ημέρα[1]

μόνο συνιστώμενος έλεγχος παρακολούθησης[1]

Το IBRANCE, 125mg μια φορά την ημέρα για 21 μέρες σε κύκλο 28 ημερών (σχήμα 3/1), ενδείκνυται για τη θεραπεία του τοπικά προχωρημένου ή μεταστατικού καρκίνου του μαστού ο οποίος είναι θετικός στους ορμονικούς υποδοχείς (HR) και αρνητικός στον υποδοχέα τύπου 2 του ανθρώπινου επιδερμικού αυξητικού παράγοντα (HER2):
- σε συνδυασμό με αναστολέα της αρωματάσης
- σε συνδυασμό με φουλβεστράντη σε γυναίκες που έχουν λάβει προηγούμενη ενδοκρινική θεραπεία

Σε προ- ή περι-εμμηνοπαυσιακές γυναίκες η ενδοκρινική θεραπεία πρέπει να συνδυάζεται με LHRH αγωνιστή.[1]

Για το πλήρες κείμενο της δοσολογίας και του τρόπου χορήγησης συμβουλευθείτε την Περίληψη Χαρακτηριστικών του Προϊόντος που διατίθεται από την εταιρεία.

PP-IBR-GRC-0063-MAY20

ΣΗΜΑΝΤΙΚΕΣ ΠΛΗΡΟΦΟΡΙΕΣ ΑΣΦΑΛΕΙΑΣ

Το Ibrance αντενδείκνυται σε περιπτώσεις υπερευαισθησίας στη δραστική ουσία ή σε κάποιο από τα έκδοχα, καθώς και σε ασθενείς οι οποίοι λαμβάνουν σκευάσματα που περιέχουν υπερικό/βαλσαμόχορτο (St. John's Wort). Οι πιο συχνές ανεπιθύμητες ενέργειες (≥ 20%) οποιασδήποτε βαθμού που αναφέρθηκαν σε ασθενείς που έλαβαν palbociclib σε τυχαιοποιημένες κλινικές μελέτες ήταν ουδετεροπενία, λοιμώξεις, λευκοπενία, κόπωση, ναυτία, στοματίτιδα, αναιμία, διάρροια, αλωπεκία και θρομβοπενία. Οι πιο συχνές (≥ 2%) ανεπιθύμητες ενέργειες Βαθμού ≥ 3 του palbociclib ήταν ουδετεροπενία, λευκοπενία, λοιμώξεις, αναιμία, αυξημένη ασπαρτική αμινοτρανσφεράση (AST), κόπωση και αυξημένη αμινοτρανσφεράση της αλανίνης (ALT).[1]

CDK4/6 = Κυκλίνο-εξαρτώμενες κινάσες 4/6, LHRH = ορμόνη απελευθέρωσης της ωχρινοτρόπου ορμόνης

Παραπομπές: 1. IBRANCE® Περίληψη Χαρακτηριστικών Προϊόντος, 02/2020. **2.** Kim ES, et al. Target Oncol. 2017;12(3):373-383. **3.** Finn RS, et al. N Engl J Med. 2016;375(20):1925-1936. **4.** Cristofanilli M, et al. Lancet Oncol. 2016;17(4):425-439.

Η συντετμημένη Περίληψη Χαρακτηριστικών του Προϊόντος δημοσιεύεται σε άλλη σελίδα του παρόντος

Βοηθήστε να γίνουν τα φάρμακα πιο ασφαλή και Αναφέρετε ΟΛΕΣ τις ανεπιθύμητες ενέργειες για ΟΛΑ τα φάρμακα Συμπληρώνοντας την «ΚΙΤΡΙΝΗ ΚΑΡΤΑ»

Pfizer Oncology

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IBRANCE®
palbociclib

ΣΥΝΤΕΤΜΗΜΕΝΗ ΠΕΡΙΛΗΨΗ ΤΩΝ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ ΤΟΥ ΠΡΟΪΟΝΤΟΣ

▼Το φάρμακο αυτό τελεί υπό συμπληρωματική παρακολούθηση. Αυτό θα επιτρέψει το γρήγορο προσδιορισμό νέων πληροφοριών ασφάλειας. Ζητείται από τους επαγγελματίες υγείας να αναφέρουν οποιεσδήποτε πιθανολογούμενες ανεπιθύμητες ενέργειες. Βλ. παράγραφο *«Ανεπιθύμητες Ενέργειες»* για τον τρόπο αναφοράς ανεπιθύμητων ενεργειών.

IBRANCE (palbociclib) ΣΚΛΗΡΑ ΚΑΨΑΚΙΑ 75 mg, 100 mg και 125 mg

ΑΝΤΕΝΔΕΙΞΕΙΣ: Υπερευαισθησία στη δραστική ουσία ή σε κάποιο από τα έκδοχα. Χρήση σκευασμάτων που περιέχουν υπερικό/βαλσαμόχορτο (St. John's Wort). **ΕΙΔΙΚΕΣ ΠΡΟΕΙΔΟΠΟΙΗΣΕΙΣ ΚΑΙ ΠΡΟΦΥΛΑΞΕΙΣ ΚΑΤΑ ΤΗ ΧΡΗΣΗ:** Προ/περιεμμηνοπαυσιακές γυναίκες. Όταν το IBRANCE χορηγείται σε προ/περιεμμηνοπαυσιακές γυναίκες σε συνδυασμό με αναστολέα αρωματάσης, είναι υποχρεωτική η ωοθηκεκτομή ή η καταστολή της λειτουργίας των ωοθηκών με χορήγηση αγωνιστή LHRH, λόγω του μηχανισμού δράσης των αναστολέων της αρωματάσης. Ο συνδυασμός του palbociclib με τη φουλβεστράντη σε προ/περιεμμηνοπαυσιακές γυναίκες έχει μελετηθεί μόνο σε συνδυασμό με ένα αγωνιστή LHRH. Κρίσιμη σπλαγχνική νόσος. Η αποτελεσματικότητα και ασφάλεια του palbociclib δεν έχουν μελετηθεί σε ασθενείς με κρίσιμη σπλαγχνική νόσο. Αιματολογικές διαταραχές. Για ασθενείς που εμφανίζουν ουδετεροπενία Βαθμού 3 ή 4 συνιστάται διακοπή της δόσης, μείωση της δόσης ή καθυστέρηση στην έναρξη των κύκλων της θεραπείας. Θα πρέπει να διεξάγεται κατάλληλη παρακολούθηση (βλ. παράγραφο *«Ανεπιθύμητες Ενέργειες»*). Διάμεση πνευμονοπάθεια/πνευμονίτιδα. Μπορεί να παρουσιαστεί βαριάς μορφής, απειλητική για τη ζωή ή θανατηφόρα ILD ή/και πνευμονίτιδα σε ασθενείς που έλαβαν θεραπεία με IBRANCE, όταν λαμβάνεται σε συνδυασμό με ενδοκρινική θεραπεία. Σε κλινικές δοκιμές (PALOMA-1, PALOMA-2, PALOMA-3), το 1,4% των ασθενών που έλαβαν θεραπεία με το IBRANCE παρουσίασε ILD/πνευμονίτιδα οποιουδήποτε βαθμού, 0,1% παρουσίασε βαθμού 3, ενώ δεν αναφέρθηκαν περιπτώσεις βαθμού 4 ή θανατηφόρες περιπτώσεις. Επιπλέον περιπτώσεις ILD/πνευμονίτιδας έχουν παρατηρηθεί μετά την κυκλοφορία στην αγορά, με την αναφορά θανατηφόρων περιστατικών (βλ. παράγραφο *«Ανεπιθύμητες Ενέργειες»*). Παρακολουθήστε τους ασθενείς για πνευμονικά συμπτώματα ενδεικτικά ILD/πνευμονίτιδας (π.χ. υποξία, βήχας, δύσπνοια). Σε ασθενείς που παρουσιάζουν νέα ή επιδεινούμενα αναπνευστικά συμπτώματα και υπάρχει η υποψία ανάπτυξης ILD/πνευμονίτιδας, διακόψτε το IBRANCE αμέσως και αξιολογήστε τον ασθενή. Διακόψτε οριστικά το IBRANCE σε ασθενείς με βαριάς μορφής ILD ή πνευμονίτιδα. Λοιμώξεις. Καθώς το IBRANCE έχει μυελοκατασταλτικές ιδιότητες, μπορεί να προδιαθέσει τους ασθενείς για λοιμώξεις. Λοιμώξεις έχουν αναφερθεί σε υψηλότερο ποσοστό σε ασθενείς που έλαβαν θεραπεία με το IBRANCE σε τυχαιοποιημένες κλινικές μελέτες σε σύγκριση με ασθενείς που έλαβαν θεραπεία στο αντίστοιχο σκέλος σύγκρισης. Λοιμώξεις Βαθμού 3 και Βαθμού 4 εμφανίστηκαν αντίστοιχα στο 4,5% και το 0,7% των ασθενών που έλαβαν θεραπεία με το IBRANCE σε οποιονδήποτε συνδυασμό (βλ. παράγραφο *«Ανεπιθύμητες Ενέργειες»*). Οι ασθενείς θα πρέπει να παρακολουθούνται για σημεία και συμπτώματα λοίμωξης και τα οποία θα πρέπει να αντιμετωπίζονται σύμφωνα με τις ιατρικές ενδείξεις. Οι γιατροί θα πρέπει να ενημερώσουν τους ασθενείς ώστε να αναφέρουν αμέσως οποιαδήποτε επεισόδια πυρετού. Ηπατική δυσλειτουργία. Χορηγήστε το IBRANCE με προσοχή σε ασθενείς με μέτρια ή σοβαρή ηπατική δυσλειτουργία, υπό στενή παρακολούθηση για σημεία τοξικότητας. Νεφρική δυσλειτουργία. Χορηγήστε το IBRANCE με προσοχή σε ασθενείς με μέτρια ή σοβαρή νεφρική δυσλειτουργία, υπό στενή παρακολούθηση για σημεία τοξικότητας. Ταυτόχρονη θεραπεία με αναστολείς ή επαγωγείς του CYP3A4. Οι ισχυροί αναστολείς του CYP3A4 μπορεί να οδηγήσουν σε αυξημένη τοξικότητα. Θα πρέπει να αποφεύγεται η ταυτόχρονη χρήση ισχυρών αναστολέων του CYP3A κατά τη διάρκεια της θεραπείας με το palbociclib. Το ενδεχόμενο συγχορήγησης θα πρέπει να εξετάζεται μόνο μετά από προσεκτική αξιολόγηση των δυνητικών οφελών και κινδύνων. Εάν η συγχορήγηση με ισχυρό αναστολέα του CYP3A δεν μπορεί να αποφευχθεί, μειώστε τη δόση του IBRANCE στα 75 mg μία φορά την ημέρα. Όταν διακοπεί ο ισχυρός αναστολέας, αυξήστε τη δόση του IBRANCE (μετά από 3 – 5 ημιπεριόδους ζωής του αναστολέα) έως τη δόση που χρησιμοποιείτο πριν την έναρξη του ισχυρού αναστολέα του CYP3A. Η συγχορήγηση επαγωγέων του CYP3A μπορεί να οδηγήσει σε μειωμένη έκθεση στο palbociclib και κατά συνέπεια σε κίνδυνο έλλειψης αποτελεσματικότητας. Συνεπώς, η ταυτόχρονη χρήση του palbociclib με ισχυρούς επαγωγείς του CYP3A4 θα πρέπει να αποφεύγεται. Δεν απαιτείται καμία προσαρμογή της δόσης για τη συγχορήγηση του palbociclib με μέτριους επαγωγείς του CYP3A. Γυναίκες σε αναπαραγωγική ηλικία ή οι σύντροφοί τους. Γυναίκες σε αναπαραγωγική ηλικία ή οι άνδρες σύντροφοί τους πρέπει να χρησιμοποιούν μία μέθοδο αντισύλληψης υψηλής αποτελεσματικότητας ενώ παίρνουν το IBRANCE. Λακτόζη. Αυτό το φαρμακευτικό προϊόν περιέχει λακτόζη. Οι ασθενείς με σπάνια κληρονομικά προβλήματα δυσανεξίας στη γαλακτόζη, έλλειψη λακτάσης Lapp ή κακή απορρόφηση γλυκόζης-γαλακτόζης δεν θα πρέπει να πάρουν αυτό το φάρμακο. **ΑΝΕΠΙΘΥΜΗΤΕΣ ΕΝΕΡΓΕΙΕΣ:** Περίληψη του προφίλ ασφάλειας. Το συνολικό προφίλ ασφάλειας του IBRANCE βασίζεται σε συγκεντρωτικά δεδομένα από 872 ασθενείς που έλαβαν palbociclib σε συνδυασμό με ενδοκρινική θεραπεία (N = 527 σε συνδυασμό με λετροζόλη και N = 345 σε συνδυασμό με φουλβεστράντη) σε τυχαιοποιημένες κλινικές μελέτες σε HR-θετικό, HER2-αρνητικό προχωρημένο ή μεταστατικό καρκίνο του μαστού. Οι πιο συχνές ανεπιθύμητες ενέργειες (≥ 20%) οποιουδήποτε βαθμού που αναφέρθηκαν σε ασθενείς που έλαβαν palbociclib σε τυχαιοποιημένες κλινικές μελέτες ήταν ουδετεροπενία, λοιμώξεις, λευκοπενία, κόπωση, ναυτία, στοματίτιδα, αναιμία, διάρροια, αλωπεκία και θρομβοπενία. Οι πιο συχνές (≥ 2%) ανεπιθύμητες ενέργειες Βαθμού ≥ 3 του palbociclib ήταν ουδετεροπενία, λευκοπενία, λοιμώξεις, αναιμία, αυξημένη ασπαρτική αμινοτρανσφεράση (AST), κόπωση και αυξημένη αμινοτρανσφεράση της αλανίνης (ALT). Μειώσεις της δόσης ή τροποποιήσεις της δόσης λόγω οποιασδήποτε ανεπιθύμητης ενέργειας αναφέρθηκαν στο 38,4% των ασθενών που έλαβαν το IBRANCE σε τυχαιοποιημένες κλινικές μελέτες ανεξαρτήτως συνδυασμού. Οριστική διακοπή λόγω ανεπιθύμητης ενέργειας αναφέρθηκε στο 5,2% των ασθενών που έλαβαν το IBRANCE σε τυχαιοποιημένες κλινικές μελέτες ανεξαρτήτως συνδυασμού. Παρακάτω αναφέρονται οι ανεπιθύμητες ενέργειες από το συγκεντρωτικό σύνολο δεδομένων 3 τυχαιοποιημένων μελετών. Η διάμεση διάρκεια της θεραπείας με palbociclib στο συγκεντρωτικό σύνολο δεδομένων κατά την τελική ανάλυση της συνολικής επιβίωσης (OS) ήταν 14,8 μήνες. Οι ανεπιθύμητες ενέργειες παρατίθενται ανά κατηγορία συχνότητας. Οι κατηγορίες συχνότητας ορίζονται ως ακολούθως: πολύ συχνές (≥ 1/10), συχνές (≥ 1/100 έως < 1/10) και όχι συχνές (≥ 1/1.000 έως < 1/100). **Προτιμώμενος όρος**[α] *Πολύ συχνές:* Λοιμώξεις[β], ουδετεροπενία[γ], λευκοπενία[δ], αναιμία[ε], θρομβοπενία[στ], μειωμένη όρεξη, στοματίτιδα[ζ], ναυτία, διάρροια, έμετος, εξάνθημα[η], αλωπεκία, ξηροδερμία, κόπωση, εξασθένιση, πυρεξία, ALT αυξημένη, AST αυξημένη. *Συχνές:* Εμπύρετη ουδετεροπενία, δυσγευσία, όραση θαμπή, δακρύρροια αυξημένη, ξηροφθαλμία, επίσταξη, ILD/πνευμονίτιδα[*,θ]. ALT= αμινοτρανσφεράση της αλανίνης, AST= ασπαρτική αμινοτρανσφεράση, ILD=διάμεση πνευμονοπάθεια, N/n = αριθμός ασθενών. N/A=δεν εφαρμόζεται. *Ανεπιθύμητη αντίδραση στο φάρμακο (Adverse Drug Reaction, ADR) που εντοπίζεται μετά την κυκλοφορία στην αγορά. [α]Οι προτιμώμενοι όροι (PT, Preferred Terms) αναγράφονται σύμφωνα με το MedDRA 17.1. [β]Οι λοιμώξεις περιλαμβάνουν όλους τους PT που αποτελούν μέρος της Κατηγορίας Οργανικού Συστήματος «Λοιμώξεις και παρασιτώσεις». [γ]Η ουδετεροπενία περιλαμβάνει τους ακόλουθους PT: Ουδετεροπενία, Αριθμός ουδετεροφίλων μειωμένος. [δ]Η λευκοπενία περιλαμβάνει τους ακόλουθους PT: Λευκοπενία, Αριθμός λευκοκυττάρων μειωμένος. [ε]Η αναιμία περιλαμβάνει τους ακόλουθους PT: Αναιμία, Αιμοσφαιρίνη μειωμένη, Αιματοκρίτης μειωμένος. [στ]Η θρομβοπενία περιλαμβάνει τους ακόλουθους PT: Θρομβοπενία, Αριθμός αιμοπεταλίων μειωμένος. [ζ]Η στοματίτιδα περιλαμβάνει τους ακόλουθους PT: Αφθώδης στοματίτιδα, Χειλίτιδα, Γλωσσίτιδα, Γλωσσοδυνία, Εξέλκωση του στόματος, Φλεγμονή βλεννογόνου, Άλγος του στόματος, Στοματοφαρυγγική δυσφορία, Στοματοφαρυγγικό άλγος, Στοματίτιδα. [η]Το εξάνθημα περιλαμβάνει τους ακόλουθους PT: Εξάνθημα, Κηλιδοβλατιδώδες εξάνθημα, Κνησμώδες εξάνθημα, Ερυθηματώδες εξάνθημα, Βλατιδώδες εξάνθημα, Δερματίτιδα, Δερματίτιδα ομοιάζουσα με ακμή, Τοξικό εξάνθημα δέρματος. [θ]Η ILD/πνευμονίτιδα περιλαμβάνει κάθε αναφερόμενο PT που αποτελεί μέρος του Τυποποιημένου Ερωτήματος MedDRA για τη διάμεση πνευμονοπάθεια (με τη στενή έννοια). Στον παρακάτω Πίνακα αναφέρονται οι εργαστηριακές παθολογικές τιμές που παρατηρήθηκαν σε συγκεντρωτικό σύνολο δεδομένων 3 τυχαιοποιημένων μελετών (N = 872).

	Ibrance συν λετροζόλη ή φουλβεστράντη			Σκέλη συγκριτικού παράγοντα*		
Εργαστηριακές παθολογικές τιμές	**Κάθε Βαθμού %**	**Βαθμού 3 %**	**Βαθμού 4 %**	**Κάθε Βαθμού %**	**Βαθμού 3 %**	**Βαθμού 4 %**
WBC μειωμένα	97,4	41,8	1,0	26,2	0,2	0,2
Ουδετερόφιλα μειωμένα	95,6	57,5	11,7	17,0	0,9	0,6
Αναιμία	80,1	5,6	Δ/Ι	42,1	2,3	Δ/Ι
Αιμοπετάλια μειωμένα	65,2	1,8	0,5	13,2	0,2	0,0
AST αυξημένη	55,5	3,9	0,0	43,3	2,1	0,0
ALT αυξημένη	46,1	2,5	0,1	33,2	0,4	0,0

WBC-λευκά αιμοσφαίρια, AST-ασπαρτική αμινοτρανσφεράση, ALT-αμινοτρανσφεράση της αλανίνης, N-αριθμός ασθενών, Δ/Ι-δεν ισχύει. Σημείωση: Τα αποτελέσματα των εργαστηριακών εξετάσεων βαθμολογούνται ανάλογα με τον βαθμό βαρύτητας της έκδοσης 4.0 των NCI CTCAE. * λετροζόλη ή φουλβεστράντη.

Περιγραφή επιλεγμένων ανεπιθύμητων ενεργειών. Συνολικά, ουδετεροπενία οποιουδήποτε βαθμού αναφέρθηκε σε 716 (82,1%) ασθενείς που έλαβαν IBRANCE ανεξαρτήτως συνδυασμού, με ουδετεροπενία Βαθμού 3 να έχει αναφερθεί σε 500 (57,3%) ασθενείς και ουδετεροπενία Βαθμού 4 να έχει αναφερθεί σε 97 (11,1%) ασθενείς. Ο διάμεσος χρόνος μέχρι το πρώτο επεισόδιο ουδετεροπενίας οποιουδήποτε βαθμού ήταν 15 ημέρες (12-700 ημέρες) και η διάμεση διάρκεια ουδετεροπενίας Βαθμού ≥ 3 στις 3 τυχαιοποιημένες κλινικές μελέτες ήταν 7 ημέρες. Εμπύρετη ουδετεροπενία αναφέρθηκε στο 0,9% των ασθενών που έλαβαν IBRANCE σε συνδυασμό με φουλβεστράντη και στο 1,7% των ασθενών που έλαβαν palbociclib σε συνδυασμό με λετροζόλη. Εμπύρετη ουδετεροπενία αναφέρθηκε σε περίπου 2% των ασθενών που εκτέθηκαν στο IBRANCE κατά τη διάρκεια του συνολικού κλινικού προγράμματος. Αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών. Η αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών μετά από τη χορήγηση άδειας κυκλοφορίας του φαρμακευτικού προϊόντος είναι σημαντική. Επιτρέπει τη συνεχή παρακολούθηση της σχέσης οφέλους-κινδύνου του φαρμακευτικού προϊόντος. Ζητείται από τους επαγγελματίες υγείας να αναφέρουν οποιεσδήποτε πιθανολογούμενες ανεπιθύμητες ενέργειες μέσω: **Ελλάδα:** Εθνικός Οργανισμός Φαρμάκων, Μεσογείων 284, GR-15562 Χολαργός, Αθήνα, Τηλ: + 30 21 32040380/337, Φαξ: + 30 21 06549585, Ιστότοπος: http://www.eof.gr. **Κύπρος:** Φαρμακευτικές Υπηρεσίες, Υπουργείο Υγείας, CY-1475 Λευκωσία, Φαξ: + 357 22608649, Ιστότοπος: www.moh.gov.cy/phs. **ΚΑΤΟΧΟΣ ΤΗΣ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ**: Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Βέλγιο. **ΤΟΠΙΚΟΣ ΑΝΤΙΠΡΟΣΩΠΟΣ ΣΤΗΝ ΕΛΛΑΔΑ:** Pfizer Ελλάς Α.Ε., Λ. Μεσογείων 243, 154 51 Ν. Ψυχικό, Αθήνα, Τηλ.: +30 210 6785800. **ΤΟΠΙΚΟΣ ΑΝΤΙΠΡΟΣΩΠΟΣ ΣΤΗΝ ΚΥΠΡΟ:** Pfizer Ελλάς Α.Ε. (Cyprus Branch), Λεωφόρος Αθαλάσσας 26, Κτήριο Στεφανή, 2ος Όροφος, 2018 Λευκωσία, Κύπρος, Τηλ.: +357 22 817690. **ΑΡΙΘΜΟΣ(ΟΙ) ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ**: EU/1/16/1147/001-009. **ΗΜΕΡΟΜΗΝΙΑ ΑΝΑΘΕΩΡΗΣΗΣ ΤΟΥ ΚΕΙΜΕΝΟΥ**: 02/2020. **ΛΙΑΝΙΚΗ ΚΑΙ ΝΟΣΟΚΟΜΕΙΑΚΗ ΤΙΜΗ - ΕΛΛΑΔΑ**: IBRANCE CAPS 75MG/CAP BTx21 σε PVC/PCTFE/PVC alu blister Λ.Τ.: 3.251,06€, N.T.: 2.696,93€. IBRANCE CAPS 100MG/CAP BTx21 σε PVC/PCTFE/PVC alu blister Λ.Τ.: 3.251,06€, N.T.: 2.696,93€. IBRANCE CAPS 125MG/CAP BTx21 σε PVC/PCTFE/PVC alu blister Λ.Τ.: 3.251,06€, N.T.: 2.696,93€. **ΛΙΑΝΙΚΗ ΤΙΜΗ - ΚΥΠΡΟΣ:** IBRANCE CAPSULE, HARD 100MG, PACK WITH 21 CAPS IN BLISTER(S) Λ.Τ.: 3.235,17€. IBRANCE CAPSULE, HARD 125MG, PACK WITH 21 CAPS IN BLISTER(S) Λ.Τ.: 3.235,17€. IBRANCE CAPSULE, HARD 75MG, PACK WITH 21 CAPS IN BLISTER(S) Λ.Τ.: 3.235,17€. **ΤΡΟΠΟΣ ΔΙΑΘΕΣΗΣ:** Περιορισμένη ιατρική συνταγή από ειδικό ιατρό και παρακολούθηση κατά τη διάρκεια της αγωγής.

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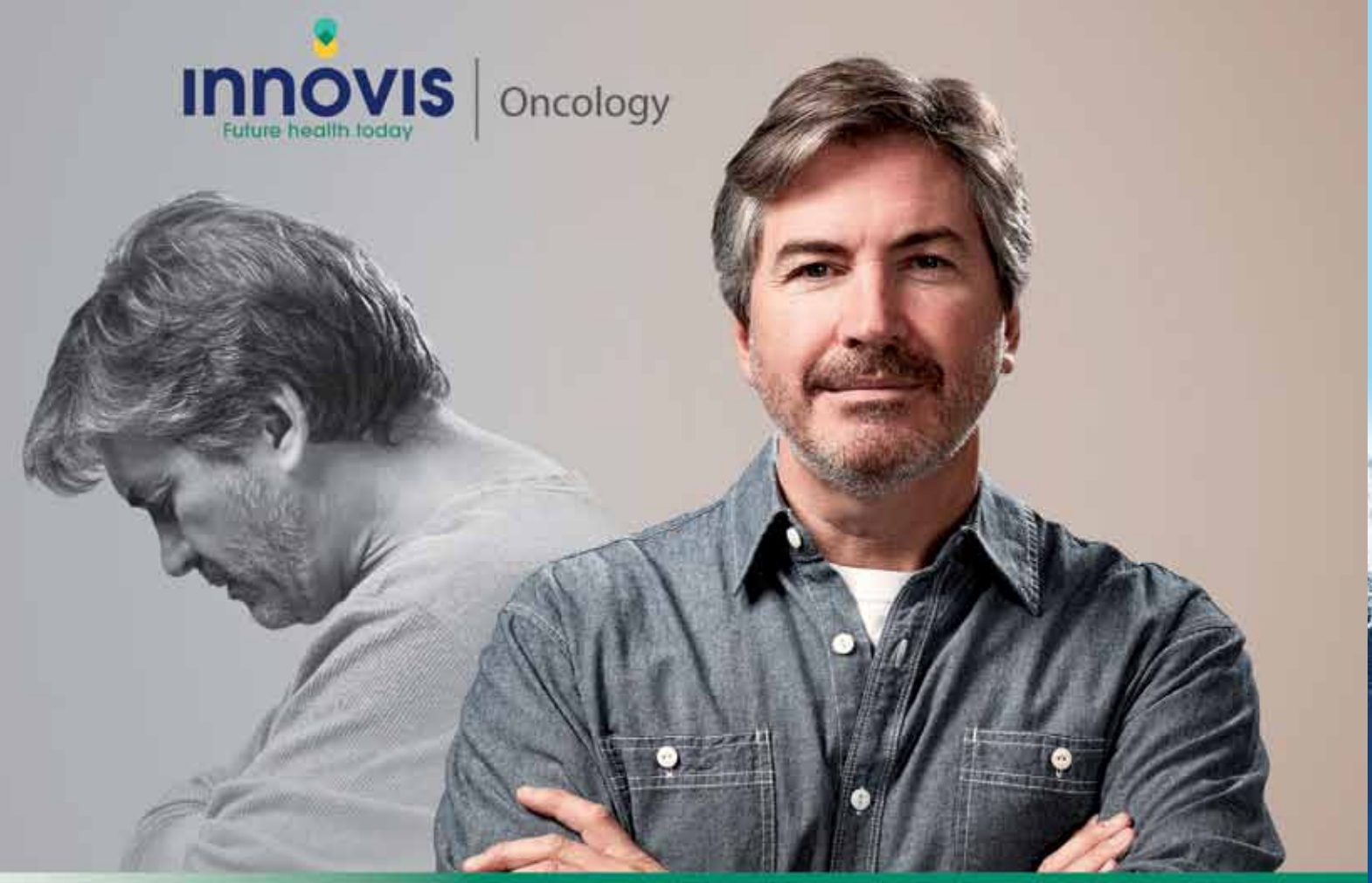

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Συνταγογραφικές πληροφορίες του προϊόντος στην σελίδα

1) Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR): final results from a randomised, open-label, phase 3 trial. The Lancet Oncology. 2016;17(7):917-27
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4) Cabometyx smpc

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για τις γυναίκες με HR+/HER2– μεταστατικό καρκίνο μαστού[1-3]

1. *Waks GA and Winer EP rev, Breast Cancer Treatment; JAMA. 2019; 321: 288-200.* **2.** *Im SA et al., Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer; N Engl J Med. 2019 Jun 4. doi: 10.1056/NEJMoa1903765,* **3.** *Slamon DJ, Neven P, Chia S, et al. Overall survival results from the phase 3 MONALEESA-3 study of fulvestrant ± ribociclib in postmenopausal patients with HR+/HER2– advanced breast cancer. Presented at: European Society for Medical Oncology Congress; September 27-October 1, 2019; Barcelona, Spain; LBA7_PR; Annals of Oncology, Volume 30, Supplement 5, October 2019*

HR+/HER2-*: θετικός σε ορμονικό υποδοχέα και αρνητικός στον υποδοχέα 2 του ανθρώπινου επιδερμικού αυξητικού παράγοντα*
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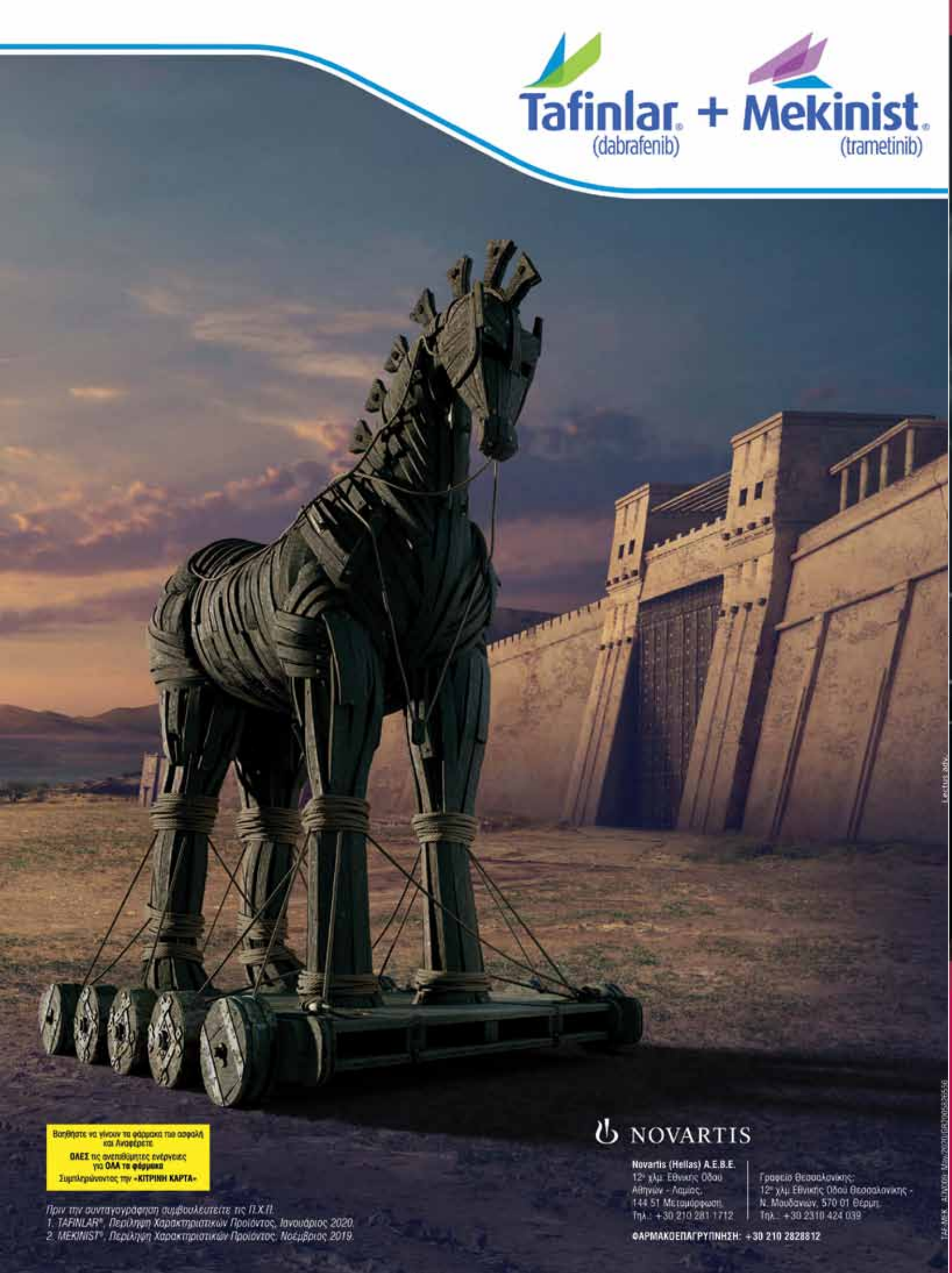

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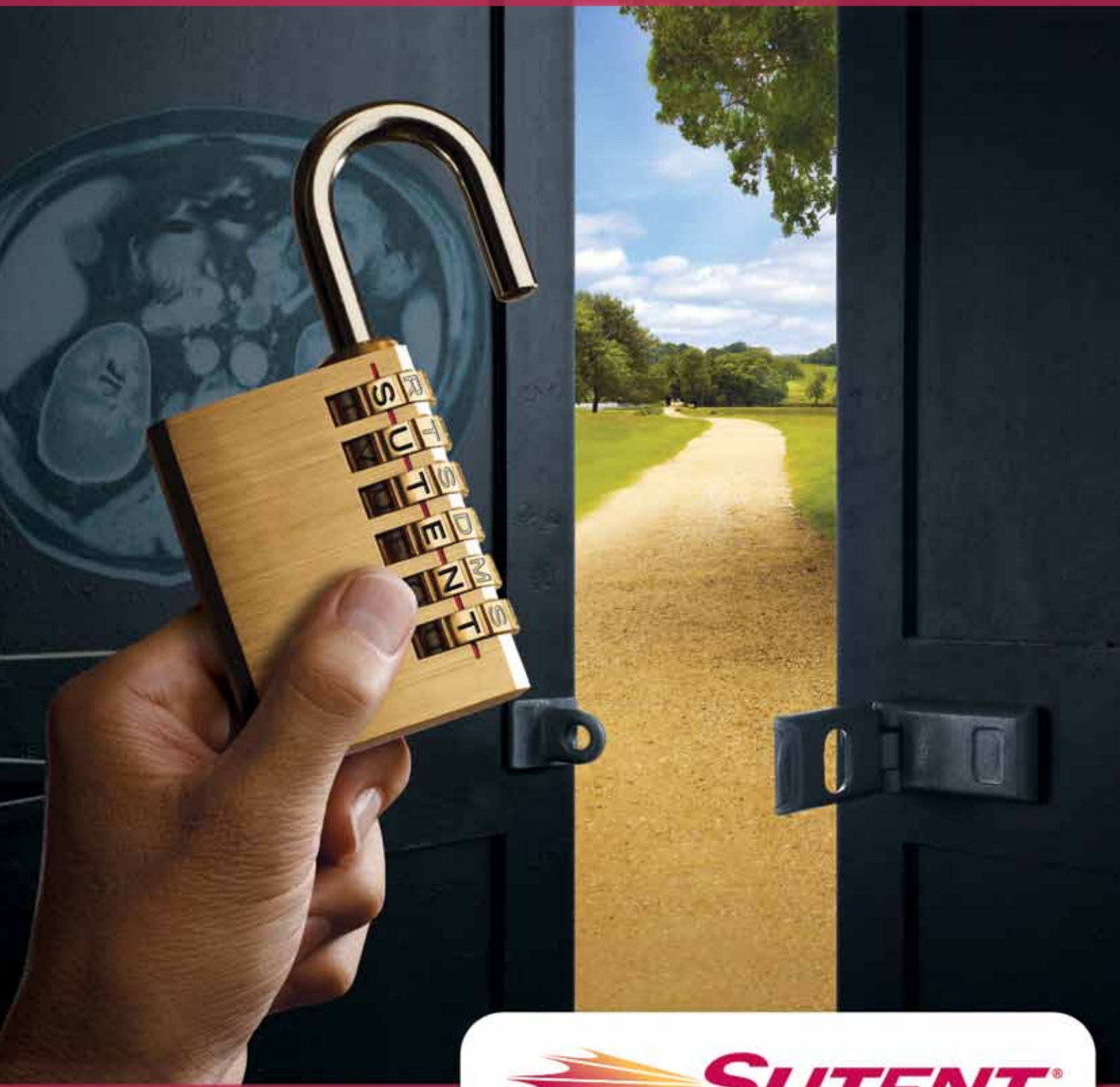

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1. Frampton GM, et al. Nat Biotechnol 2013; 31: 1023–1031. **2.** Clark TA, et al. J Mol Diagn. 2018; 20: 686–702. **3.** He J et al. Blood 2016; 127: 3004–3014. **4.** FoundationOne®CDx Technical Specifications, FoundationOne®Liquid Technical Specifications, FoundationOne®Heme Technical Specifications. Available at: www.rochefoundationmedicine.com

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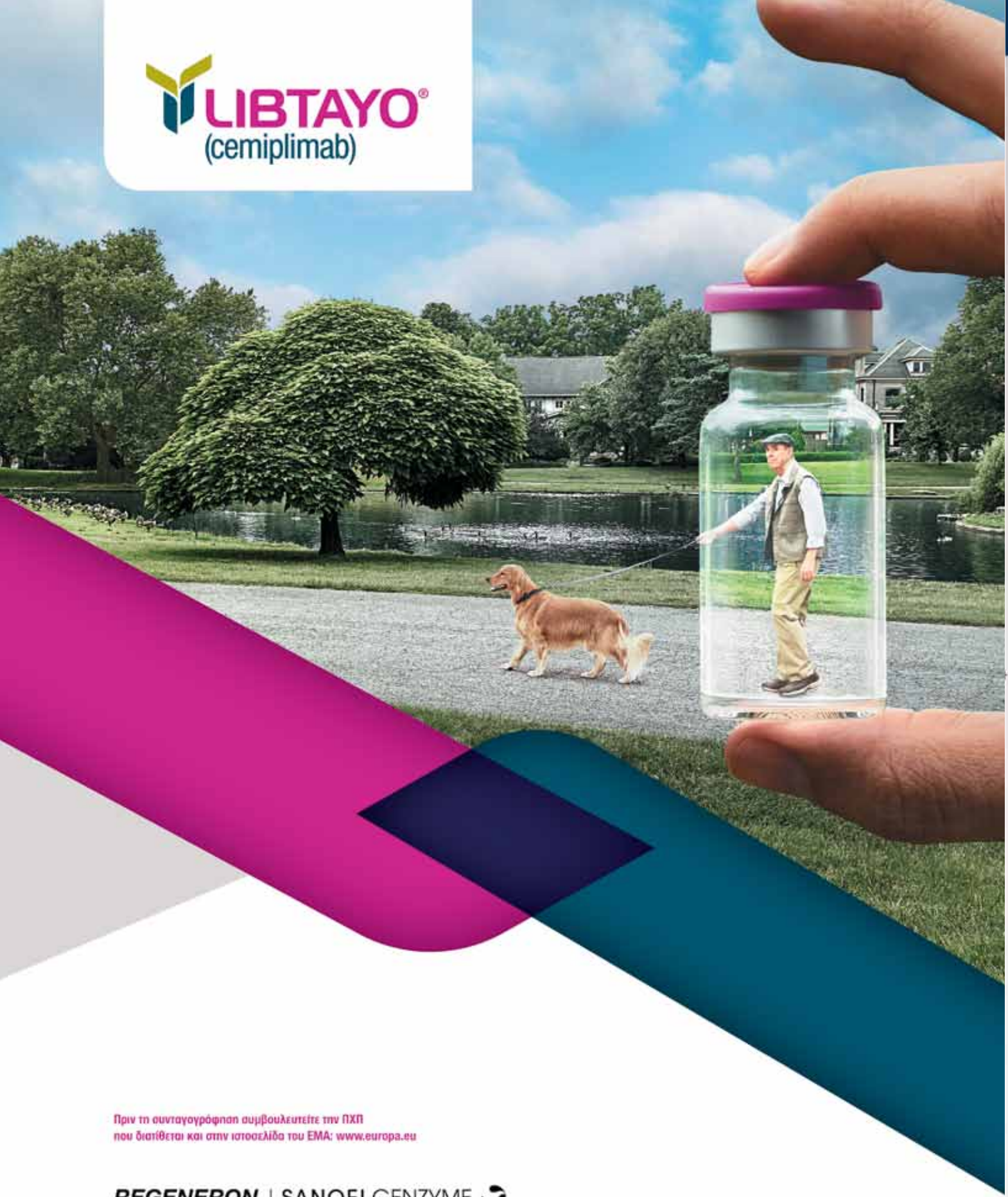

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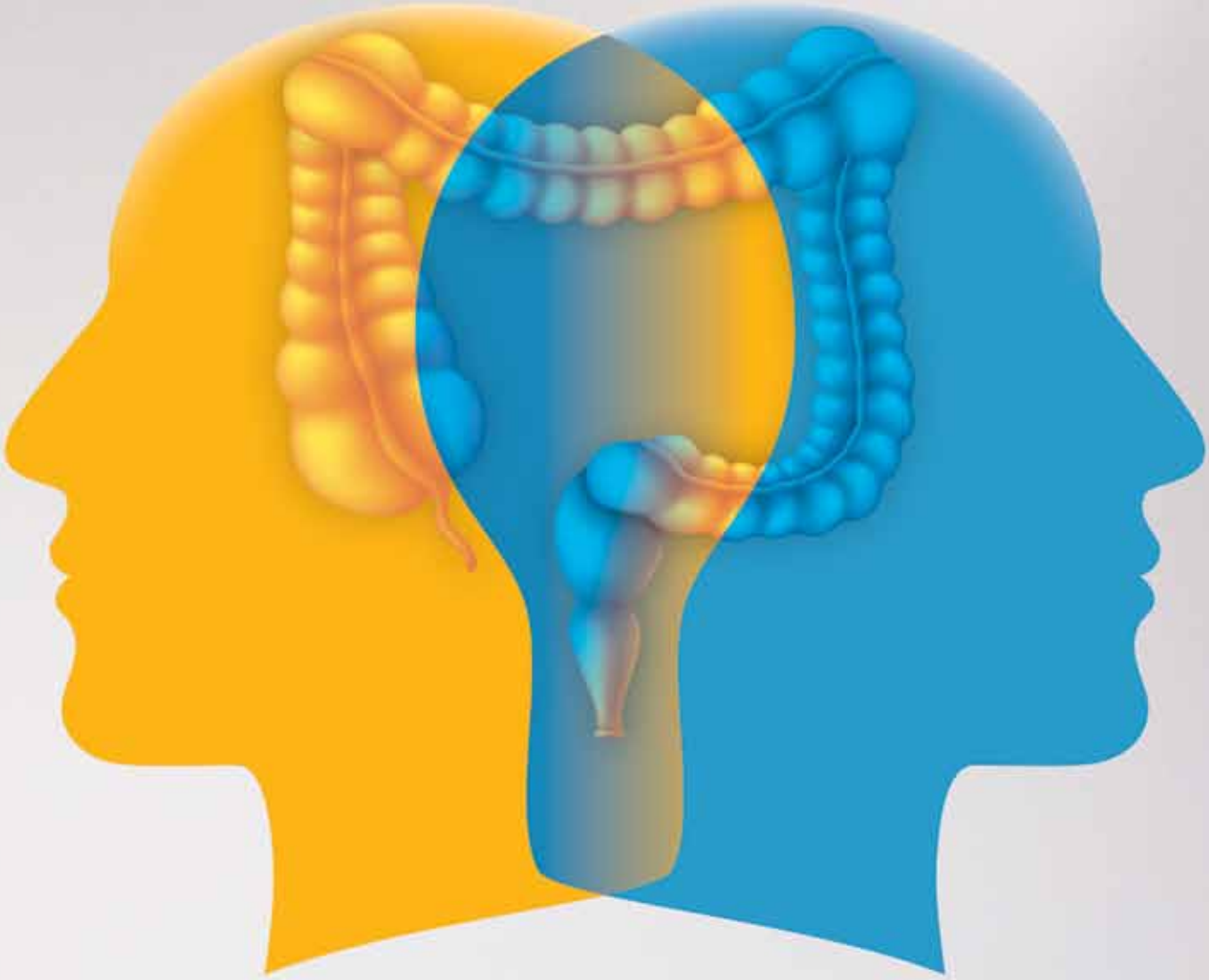

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