

POSTERS

P1 - ALK-rearranged lung non small cell carcinoma with CNS metastasis responding to alectinib: a case report

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Lung cancer remains the leading cause of cancer mortality worldwide due to advanced stage of diseases at diagnosis, but also due to modest response to therapy. The identification of molecular subtypes of NSCLC have transformed the clinical management of this disease. This is best exemplified by the clinical success of targeting, among others, the ALK mutation. Patients with NSCLC and ALK rearrangements generally have a progression-free survival of 8–11 months while on treatment with the ALK inhibitor crizotinib. However, resistance inevitably develops, with the brain a common site of progression. Alectinib is a novel, highly selective, and potent ALK inhibitor that has shown clinical activity in patients with crizotinib-naive ALK-rearranged NSCLC and with consistently demonstrable CNS activity.

We present 50-year-old never smoker male patient who was diagnosed with stage IV NSCLC. He received two lines of treatment, three cycles of carboplatin+paclitaxel, and one cycle of pemetrexed chemotherapy with partial response. During the second line of treatment we performed re-evaluation including bronchoscopy for molecular mutation testing on EGFR and ALK. His tumor tested positive for rearrangement of the anaplastic lymphoma kinase (*ALK*) gene and he started with crizotinib and achieved stable disease for 16 months. Due to neurological symptoms urgent CT scan of the brain revealed several small brain lesions so he is being treated successfully with a second-generation ALK inhibitor alectinib. That treatment has been ongoing for 4 months and on control CT brain scan we follow stable intracranial disease.

Alectinib is a second-generation ALK inhibitor well tolerated, with promising antitumour activity in patients with ALK-rearranged NSCLC resistant to crizotinib, including those with CNS metastases.

P2 - Predictors of response to neoadjuvant treatment in estrogen receptor-positive breast cancer at the University Hospital for Tumors, Sestre milosrdnice University Hospital Center; a retrospective cohort study

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Breast cancer is not a single disease, but it is made up of different subtypes of tumors that differ in their biological behavior, aggression, tendency of metastasis and response to therapy. Among the patients with early breast cancer there is a subset of a patients who, with regard to disease biology or tumor size, is at increased risk for recurrence of the disease, ie subgroup with a worse prognosis. With the aim of reducing the risk of disease recurrence, systemic therapy has been traditionally used in the adjuvant setting, ie performed following surgical treatment. For the last 20 years, neo-adjuvant or inductive systemic therapy has been increasingly used as a fundamental strategy for treating patients with early breast cancer. Studies conducted so far indicate that the clinical and pathological response is largely dependent on the subtype of breast cancer. The studies consistently showed that the response to neoadjuvant treatment (achieving complete pathological response / pCR) was significantly lower in patients with ER-positive versus ER-negative breast cancer patients.

Aim of our study was to try to create a model for early prediction of pathological full response (pCR) to neoadjuvant treatment of ER-positive breast cancer. This retrospective cohort study was performed at the University Hospital for Tumors in a consecutive sample of 48 women treated with neo-adjuvant systemic antineoplastic therapy during 2015 and 2016.

The test was performed on 68 patients. Finally, the study included 48 patients, out of which 13 (27%) received complete response to neo-adjuvant systemic antineoplastic therapy. After adjusting for all involved variables with multivariate binary logistic regression, the full response was independent, statistically significant tumor size and lymph node involvement. Patients with a tumor ≥ 2.0 cm had 99% less chance of PCR than women with tumors < 2 cm (OR = 0.01, 95% CI (0.00-0.28, $p = 0.009$). lymph nodes had a 20.7-fold higher chance for pCR than women without affected lymph nodes (OR = 20.7; 95% CI 1.19-360.67; $p = 0.038$). Predictive model with only two variables: tumor size and involvement lymph nodes were significant (Omnibus test, $p < 0.001$), well-aligned with empirical data (Hosmer's and Lemeshow's test, $p = 0.334$), relatively high predictive values (Nagelkerke $R^2 = 0.42$, 81% of the exact classifications).

Classification and regression strain revealed two segments of patients with the best prospects for pCR: 1) Patients with a tumor size < 2.0 cm including 83% of pCR; 2) Women with tumor size ≥ 2.0 cm with affected lymph nodes and HER2 negative tumor, including pCR 44%.

In conclusion, tumor size < 2 cm and lymph node involvement are promising predictors of response to neo-adjuvant systemic antineoplastic therapy of ER-positive breast cancer. The model is necessarily validated on an independent sample.

As a limitation of the study, it is to be stressed out hat the size of the available population did not allow us to validate the model on an independent sample. At the University Hospital for Tumors, a validation prospective cohort study is currently underway, which we expect to complete in April 2018. The retrospective setup of our study has prevented us from analyzing more potentially important predictors such as lymphovascular invasion, gradus, cellularity, type or tumor immunophenotype.

P3 - Treatment of platinum- and cetuximab-refractory hypopharyngeal cancer; a case report

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A 66-year old male, moderate smoker (40 p/y) with dysphagia, pain in the left ear and hoarseness lasting since September 2014 was admitted to the Department of Otorhinolaryngology, Head and Neck Surgery in December 2014. His past medical history included arterial hypertension. Ulcero-proliferative lesion in the left pyriform sinus with immobility of left vocal cord was diagnosed by fiberoptic endoscopic examination. Histological examination of the lesion biopsy showed the poorly differentiated squamous cell carcinoma. No enlarged lymph nodes and distant metastasis were detected. The patient underwent partial laryngopharyngectomy with neck dissection. The final histopathological exam reported the presence of a poorly differentiated squamous cell carcinoma (pT3pN0, G3, EGFR positive, R0). Locoregional recurrence and lung and liver metastases were identified in May 2015. The patient was included in EXTREME trial and received maximum of 6 cycles of cisplatin (at a dose of 100 mg/m² as a 1-hour intravenous infusion on day 1) and an infusion of fluorouracil (at a dose of 1000 mg/m² per day for 4 days) every 3 weeks. Cetuximab was administered at an initial dose of 400 mg/m² given as a 2-hour intravenous infusion, followed by subsequent weekly doses of 250 mg/m² given as a 1-hour intravenous infusion. Tumor response assessed by CT and MRI after 6 cycles showed progression. Then docetaxel (at a dose of 35 mg/m² as a short intravenous infusion on day 1) was administered weekly between September 2015 and November 2015. During second-line docetaxel progression of the disease was noticed. From December 1, 2015, he received metotrexate (at a dose of 40 mg/m² as a short intravenous infusion on day 1) weekly, but just 2 cycles because he developed left-side pneumonia. He was admitted to the hospital through the emergency department and intravenous broad-spectrum antibiotics were indicated. It took about 2 months for him to feel better. From February 2016 onwards, pembrolizumab (200 mg) was administered every 3 weeks. First site of disease regression were lung metastases. After 9 months of therapy with PD-1-blocking antibody slight regression of liver metastases was also observed. The patient did not report any kind of adverse reaction.

P4 - Public health significance of lung cancer in Sisak, Croatia-Moslavina County

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Lung cancer is the most common common type cancer in the Republic of Croatia and only 10,9% of cases are diagnosed in the early stage.

The aim of this paper is to compare the trends of incidence and mortality of malignant bronchus, trachea and lung neoplasm(C33, C34) in Sisak, Croatia- Moslavina County (SMC) and Republic of Croatia (RC) between the years 2000 and 2014 with purpose of developing public health interventions for timely detection of cancer.

The source of mortality data is the Croatian Bureau of Statistics and the source of incidence data is the Croatian National Cancer Registry. The results are presented as age standardised (AS) rates for total population and gender.

The results show higher average AS rates of incidence (69,4/100 000) and mortality (65,6/100 000) in SMC compared to RC (64,8/100 000; 61,7/100 000). Average male AS mortality is higher in SMC (114,9/100 000) compared to that in RC (99,8/100 000). Male incidence and mortality rates in SMC oscillate, but mortality tends to increase. Average female AS rates of incidence (24,0/ 100 000) and mortality (22,3/100 000) in SMC are lower than that in the RC (28,2/100 000; 26,2/100 000) but they tend to increase.

Considering the results, it is necessary to promote the importance of early detection and treatment of lung cancer at the population level. It is particularly important to direct educational and other health activities to high- risk individuals, to monitor the risk factors and research the quality of life and the habits of the population. Collaboration with different parts of broader community can contribute to raising awareness of this problem, better comprehensive patient care and reducing the negative effects of the disease.

P5 - Clinical and molecular characteristics of triple-negative early breast cancer patients in University Hospital Centre Zagreb

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Triple-negative breast cancer (TNBC) is defined by lack of expression of estrogen receptor, progesterone receptor and HER-2 amplification and accounts for approximately 15-20% of breast cancers. It is also a heterogeneous group of tumors which tend to have an aggressive phenotype with higher recurrence rates and lower survival rates. This subtype lacks unifying molecular alterations that can guide therapy decisions. To date, there are no approved targeted therapies specifically for this subtype; however, many are in development.

Data of 82 patients primary surgically treated at UHC Zagreb with TNBC diagnosis according to immunohistochemical and pathological criteria were collected. The analyzes are based on the parameters: age, primary tumor size, expression of Ki-67 proliferation factor, nuclear and histological grade of tumors, expression of cytokeratine 5/6, as well as the affected lymph node and angioinvasion. The collected data are statistically processed.

The examined sample consisted of 82 patients with TNBC aged 29 to 89 divided into three age groups (<39, 40 to 55 and >55). The median age of our patients is 58. The average ages of three age groups are 33, 49 and 66. According to tumor size we divided the patients according to the TNM classification in three groups: T1 (<2 cm); T2 (2-5 cm), and group T3 (>5 cm). The average tumor sizes in these three groups of patients are: 1.3 cm, 2.8 cm and 6.0 cm. The median tumor size is 2.1 cm. Statistical data analysis suggests that the younger patients have bigger primary tumor (3.4 cm), while the oldest patients have an tumor average size of 2.4 cm. Nuclear or histological grade III is mostly found in patients of all ages, regardless of tumor size. The Ki-67 proliferation index range from 8% to 95%; and its level of expression was analyzed in three age and tumor size subgroups. It was found that the patients with the largest tumors also have the highest proliferating index (Ki67). Median tumor size according to TNM classification ranges in this sequence for T1 is 1.3 cm and median Ki67 is 57%; for T2 2.8cm while the Ki67 median was 53% and for the T3 group the median tumor size was 6 cm, while the Ki67 median 72%. Only 5 patients have a proliferation index of less than 20%.

TNBC was found in women of all ages, although we have noticed that patients <39 years of age have larger tumors. In all age groups, the most prevalent are grade 3 tumors. There was a correlation between a larger proliferation index and angioinvasion with primary tumor size. Such association was not found with the involvement of the lymph nodes of the armpits.

P6 - Are we burnt out from our work? - signs of burnout in Medical Oncology residents

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Burnout is a job-related state of emotional, mental, and physical exhaustion caused by excessive and prolonged stress. Burnout reduces productivity at work, leads to loss of interest and motivation, lack of energy, feeling of helplessness, hopelessness, cynicism.

We spread an anonymous questionnaire among 25 Medical Oncology (MO) residents. The questionnaire was designed to determine burnout level based on the signs of burnout experienced since MO residents started their residency. High burnout level was defined as experience of >10 symptoms of burnout.

56% of MO residents had experienced more than 10 signs of burnout, more often in University Hospital for Tumors (75% of MO residents) than in University Hospital Centre Zagreb (38% of MO residents). Residents were mostly annoyed more easily by other people's demands and by stories about their daily activities (83%), tired more easily (79%), overloaded by great responsibility and pressure (58%), experienced physical and emotional exhaustion (50%), they were more forgetful when it comes to appointment, deadlines, personal possessions (50%) and had feeling that their work was not appreciated enough (50%). Number of patients managed/examined in a day by a resident was 30 in UHT, while in UHC Zagreb it was 11. Source of stress for majority was bad interpersonal relationship (90%).

Burnout is one of the hazards in life which can affect every area of life, including home, work, health and social life. Because it has many serious consequences, it is important to recognize and face burnout as soon as possible. Slight lifestyle modifications, changes in management, better communication among colleagues and seeking professional help may reduce burnout.

P7 – Job satisfaction in Medical Oncology residents

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Although oncology is a very rewarding profession it can be also very demanding and stressful, especially during residency.

Aim of this study was to find out whether Medical Oncology (MO) residents are satisfied with their residency.

We spread an anonymous questionnaire among 25 MO residents. The questionnaire was designed to determine job satisfactions among MO residents and factors that led to dissatisfaction. Questionnaire also included part where residents could write down their ideas for improvement of MO residency.

76% of MO residents were satisfied with their residency, only 32% of them were satisfied with salary, while 28% were thinking about quitting residency, 26% were thinking about leaving medicine, and 60% were thinking about going working abroad. Residents were mostly bothered with increased administration workload (64%), limited financial resources for patients (56%), nature of malignant disease (56%), lack of professional accomplishment (56%).

Oncology is a fast developing field of medicine which offers a lot of opportunities for enormous career satisfaction. Advances in science have improved diagnostics, therapy options, treatment outcomes and quality of life for our patients, and made oncology very exciting and intellectually stimulating. But on the other hand, oncologists are constantly faced with complexed individualized treatment decisions, providing support for patients and their family, dealing with death and suffering, administration of highly toxic therapy, keeping up with rapid scientific and treatment advances, financial restrictions, increased workload, administration and legal issues.

P8 – Our experience in management of metastatic HER2-positive breast cancer with trastuzumab emtansine

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Trastuzumab emtanzine is an antibody-drug conjugate that contains trastuzumab, a humanized monoclonal antibody covalently linked to DM1, a microtubule inhibitor, via a stable linkage. It is indicated in the second line of treatment of patients with HER2 positive, unresectable locally advanced or metastatic breast cancer in monotherapy who previously received trastuzumab and a taxane, separately or in combination.

From 05/2014. to 10/2017. at the University Hospital for Tumors, 21 patients started treatment with trastuzumab emtanzine . The median age of the patient was 59 years (28-77). The most common metastasis sites in our patients were bones (38,10%), then multiple metastatic sites (28,57%), parenchymal organs (23,81%) and lymph nodes (9,52%).

The drug was administered at a dose of 3.6 mg / kg bodyweight via intravenous infusion every 21 days, 2 patients received the drug in reduced dose (3.0 mg / kg) for initially impaired liver function at the start of treatment. 19 patients, received the drug in the second line of treatment and 2 patients in the third line of treatment for metastatic disease. Evaluation of treatment response was initially performed after 4 and then after each 6 cycles of therapy. The average number of treatment cycles received was 4 (1-22). So far diagnostic assessment has been performed in 13 patients, resulting in partial regression of the disease in 2 patients (15,39%), and stable disease in 5 patients (38,46%), 6 patients (46,15%) were diagnosed with progression of the disease. The most common site of progression were lungs (4 patients). Clinical benefit (CB) was achieved in 7 patients (53,85%). Median time without disease progression (PFS) was 2,8 months (1-18). During the treatment no grade 3 and 4 side effects were observed and the drug was well tolerated.

Based on our experience, trastuzumab emtanzine has shown to be an effective and safe agent for treating HER2 positive metastatic breast cancer.

P9 – Survival rates as moving targets: lung cancer target therapy amplifies survival expectations

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Lung cancer is the leading cause of cancer death among both men and women, and only 18% of all patients with lung cancer are alive five years or more after diagnosis. The data are even worse for metastatic, stage IV lung cancer with a 5-year survival rate about 1%.¹ Also, only 16% of lung cancers are diagnosed at a localized stage.

In not so far past, therapy options for NSCLC (non-small-cell lung cancer), and especially for metastatic NSCLC, was very modest. Thanks to driver mutations and target therapies a great revolution happened between therapy strategies for NSCLC.

In May 2016, a 66-year-old man was presented in our hospital with several week history of dyspnea, dry cough and chest pain. He also noticed a low back pain and gradual, slow, but progressive loss of sensation and muscle weakness in his legs. Initial chest X-ray showed a shadow in the upper right lung field. A computed tomography (CT) scans of the chest and abdomen revealed a large mass in the upper right bronchus measuring up to 8 cm in its larger axis, in both lungs numerous soft tissue and subpleural nodes with lymph nodes infiltrations (right hilar, mediastinal, bilateral axillar), right pleural effusion and osteolytic bone lesions in Th1 to Th12, L1 and L4 vertebral bodies. Also, there was a significant compression of the spinal cord with an osteolytic bone lesion in Th11 vertebra. Bronchoscopy indicated the presence of a large mass in the upper right bronchus and biopsy confirmed lung adenocarcinoma as a diagnosis. Based on the examination findings and bronchoscopy, the patient was diagnosed with stage IV lung adenocarcinoma. Considering neurological symptoms and spinal cord compression with metastatic lesion, the radiation treatment was performed (TD 30 Gy/10 fractions) with complete recovery of neurological symptoms. Furthermore, the patient was scheduled for a combination of chemotherapy so he received two chemotherapy cycles of paclitaxel and carboplatin. In the meantime, the EGFR positive driver mutation was identified in his tumors samples so we discontinued chemotherapy applications and in July 2016 started treatment with erlotinib in daily dose of 150 mg. Periodically follow-up by MSCT scan did not show any recurrent disease, and at the last follow-up in September 2017 MSCT thorax and abdomen was unchanged.

Our patient, who was initially diagnosed as stage IV lung adenocarcinoma and start treatment with tyrosine kinase inhibitor erlotinib, from July 2016 until today, so far for 16 months, according to his clinical presentation and MSCT findings, has not any recurrent disease.

In this relatively short period target therapy significantly improved clinical outcome in metastatic NSCLC. There are newer agents for lung cancer, in addition to chemotherapy - targeted therapy and immunotherapy, and we expect a further significant improvement in the clinical outcome for lung cancer.

P10 – An unusual case of rhabdomyosarcoma as anterior mediastinal mass, in the clinical presentation of Superior Vein Cava Syndrome

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Sarcomas are rarely thoracic tumors, can originate from lungs, mediastinum, pleura or thoracic wall itself. Since these tumors remain clinically silent, often reach large dimensions before they are diagnosed.

49-year-old male patient was hospitalized at our Center due to dyspnea and chest pain lasting for months. Previously he was observed at General hospital where radiologic finding (MSCT) was expansive process of mediastinum with infiltration of the Vena Cava Superior, compression of the trachea with minimal pleural effusion. Upon arrival the patients symptoms corresponded to the presentation of Superior Vena Cava Syndrome, along with radiologic signs of pleural effusion progression. Chest drainage was performed, but cytological there was no evidence of malignant cells. Analised samples reached by bronchoscopy were also without evidence of malignancy. We accessed CT-guided percutaneous transthoracic biopsy, and histopathological specimen examination provide diagnosis of sarcoma, without a clear differentiation. These samples were processed at an external foreign institution, and diagnosis was Rhabdomyosarcoma, pleomorphic subtype. Immunohistochemistry was a positive to the desmina, SMA, Myo FD5; STAT6 . By decision of the Oncology Team for mesenchymal tumors, a differential oncology treatment is indicated. Immediate tumor irradiation was performed, and then patient received the 1st cycle of chemotherapy according to protocol MAID. After the first chemotherapy cycle, due to bilateral pneumonia patient dies.

The Rhabdomyosarcoma is bimodal , occurs in children and in the adult over the age of 50, mostly men. Non-specific in clinical appearance (cough, chest pain, dyspnea). Usually diagnosed late, like large mass. Prognosis is poor.

P11 - Pericardial effusion as the first manifestation of locally advanced pulmonary adenocarcinoma in emergency services; case report

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Pericardial effusion(PE) is common in malignant disease. It can result from direct tumor infiltration in advanced disease, be a consequence of therapy or be the first manifestation of malignant disease, most frequently caused by lung and breast tumors⁽¹⁾. Smaller chronic PE cause unspecific symptoms (dyspnoea, cough, chest discomfort, palpitations, syncope). If abrupt, even small amounts of fluid (eg 100 ml) can cause cardiac tamponade and death. Good clinical assessment, immediate heart ultrasound (HUS) and pericardiocentesis are the most important procedures in acute care that improve the short term survival.

We present the case of a previously healthy male treated in emergency department(ED) for malignant PE and threatening cardiac tamponade as the first manifestation of adenocarcinoma of the lungs. Symptoms and signs of PE were initially overlapped with respiratory infection, and clarity of the clinical image, targeted diagnosis and treatment started only after he was admitted in the ED in the state of threatening cardiac tamponade. After emergency HUS, pericardiocentesis and fluid evacuation, we confirmed chronic malignant PE (adenocarcinoma) and patient symptoms were diminishing. He was then transferred to specialty clinic for further treatment.

PE and cardiac tamponade may appear to be the first manifestations of malignancy. The development of cardiac tamponade is an emergency with a high risk of death. Expert clinical assessment of the patients' emergency status, recognition of the malignant disease as a possible etiologic factor, as well as valid timely indication for urgent HUS and pericardiocentesis are the most important steps in acute care of these patients.

P12 - Comparative effectiveness of nab-paclitaxel plus gemcitabine vs gemcitabine plus cisplatin or gemcitabine alone for the first-line treatment of pancreatic adenocarcinoma in the University Hospital Centre Zagreb

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The goal of this non-randomized, retrospective, and observational study was to assess the efficacy of three different first-line chemotherapy regimens in the treatment of pancreatic cancer. Data were retrieved on 130 patients (pts) who were treated for pancreatic cancer in the University Hospital Centre Zagreb between December 31st, 2014 and July 1st, 2017. Pts were treated with nab-paclitaxel plus gemcitabine (Nab-Gem), gemcitabin plus cisplatin (Cis-Gem), or gemcitabin alone (Gem). Median age at the time of the beginning of therapy was 61.5 yrs in the Nab-Gem group (n=36), 64.4 yrs in the Cis-Gem group (n=19), and 70 yrs in the Gem group (n=75).

The median duration of treatment for Nab-Gem, Cis-Gem, and Gem regimens was 14.3, 24.7, and 12.9 weeks (w), respectively. Multivariate analyses tested influence of prognostic factors on treatment duration. In accordance with previous studies, for the pts treated with Nab-Gem the duration of treatment was negatively correlated with age ($p < 0.05$). The same age-dependent relationship was not observed in the Cis-Gem and Gem groups. Pts treated with Nab-Gem showed significant difference in terms of time to failure of treatment when analyzed for the two age groups separately, <65 and >65 yrs of age. The <65 group received chemotherapy for the median duration of 21.1 w compared to the >65 group which was treated with Nab-Gem for median of 10 w. No significant sex-dependent difference was found in regard to duration of treatment in any of the three treatment regimen groups.

The fact that Nab-Gem regimen was exclusively used to treat metastatic disease undoubtedly had negative impact on the treatment result compared to other two treatment options which were used for localised inoperable disease as well as metastatic.

With regards to the above limitations of the study, we conclude that, for selected patients, a combined use of Cis-Gem is superior to Gem alone in the first-line treatment for inoperable and/or metastatic pancreatic cancer. Furthermore, with optimal selection of pts, Nab-Gem is an effective chemotherapy regimen with significant clinical effect.

P13 – Do patients from routine practice reflect clinical study population? First line treatment of metastatic HER2 positive breast cancer in University Clinical Centre Zagreb

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Thanks to the Cleopatra study, the dual HER2 blockade together with chemotherapy has become the standard of first line treatment for HER2-positive metastatic breast cancer.

We analyzed and compared clinicopathological characteristics (age, metastases sites and hormone receptor status) between a cohort of women included in Cleopatra study and our cohort of women with HER2-positive metastatic breast cancer treated with trastuzumab, pertuzumab and chemotherapy.

Mean age of 34 our patients was 54.5 years, while 10 (29.40%) of them were older than 65, and 2 of them were older than 75 years (5.88%). At Cleopatra study, mean age of 808 patients was 53.5 years and 127 (15.72%) of them were older than 65 while 19 (2.35%) of them were older than 75 years.

Adjuvant trastuzumab had received 18 (52.94%) of our patients compared to 376 (46.53%) patients from the Cleopatra study cohort.

In our study cohort, we had 10 women (29.40%) with bone metastases and 24 (70.60%) with visceral metastases, while in the Cleopatra study cohort there were 178 (22.03%) women with bone, and 630 (77.97%) women with visceral metastases.

Also, hormone receptor status was positive in 24 (70.60%) patients from our study cohort and in 388 (48.02%) patients from the Cleopatra study cohort.

When we compare clinicopathological characteristics of these two cohorts we can conclude that our cohort had more patients older than 65 and also older than 75 years. Furthermore, our cohort has more women with hormone receptor positive breast cancers in comparison to the Cleopatra study cohort.

We will continue collecting and tracking patients because these are too small numbers to definitely conclude that the patients from everyday practice have different clinical and pathological characteristics compared to the study population.

P14 - The meaning of positive surgical margins in patients whom partial nephrectomy has been made because of kidney cancer

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Positive surgical margins occurs on final pathological evaluation in certain percent of patients, whom nephron- sparing surgery has been made, because of kidney cancer.

One study which included 1344 patients, whom partial nephrectomy has been made because of kidney cancer, found that 5,5% of them had positive surgical margins. In this study patients with positive margins had the same frequency (2-3%) of local relapse of the disease, during the 5 years of tracking, as the ones whom surgical margins were negative. Both groups also had the same incidence of distant metastasis (5%). In another study, which included 1240 patients whom partial nephrectomy has been made because of kidney cancer, positive surgical margins were found in 7,8 % of them. In this particular study positive surgical margins has been associated with more frequent relapse of the disease, in patients with high risk of recurrence (pT2-pT3; Fuhrman grade III-IV). In patients who had low risk of relapse (pT1; Fuhrman grade I-II), positive surgical margins were not associate with the frequency of recurrence.

Conclusion: Average risk of local relapse after partial nephrectomy, in patients with kidney cancer with positive surgical margins, is relatively low. The authors recommends surveillance of these patients regardless of the margin status! Other options would include repeat excision, radical nephrectomy or thermal ablation.

P15 - Doege-Potter syndrome: hypoglycemia secondary to solitary fibrous tumors; case report

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Paraneoplastic syndrome is a group of symptoms and signs caused by substances that are synthesized by the tumor, or are the result of a tumor response. Solitary Fibrous Tumor (SFT) is a heterogeneous group of benign and malignant tumors from fibroblast-like cells. It represents 2% of all soft tissue tumors. Doege-Potter syndrome is a paraneoplastic hypoglycemia caused by an increased level of Insulin growth like factor (IGF-II), which increases glucose uptake in the muscle and decreases liver cell gluconeogenesis. It occurs in 12-13% of malignant but also benign SFT. The best therapy is the surgical resection of the tumor. It can also be treated with corticosteroids. We will present male patient born 1983. In June 2017, the patient was hospitalized at a local hospital due to recurrent syncope and dizziness. Diagnostic work up discovered hypoglycemia up to 1.6 mmol/L with large 15.5x11x15 cm tumor in pelvis with infiltration of pelvic bones and metastases of liver and pulmonary parenchyma. Surgical biopsy was performed. PHD (KBC Zagreb) confirmed the diagnosis of malignant fibrous solitary tumor. The patient was transferred to KBC Zagreb for the onset of oncological treatment. Initial hypoglycemiae were partially corrected by 10% glucose infusions. The endocrinologist, considering the decreased insulin and c-peptide values, concluded that it is probably paraneoplastic hypoglycaemia caused by elevated IGF-II. Therapy with methylprednisolone was introduced which resulted with no further hypoglycemia and the patient became independent of parenteral glucose. Level of IGF-II was normal in external laboratory. This is expected since therapy was introduced earlier and blood was not taken during hypoglycemia. We started chemotherapy with MAID protocol (doxorubicin, ifosfamide, dacarbazine). First radiological re-evaluation showed stable disease. The patient is in good clinical condition and has no limits in everyday life. This case is a good illustration of the variety of clinical manifestations of mesenchymal tumors. In such cases, cooperation between institutions as well as interdisciplinary collaboration within the institution through multidisciplinary teams is crucial.

P16 - Prognostic value of lymphovascular invasion (LVI) in breast cancer patients with clinically node-negative axilla

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Breast cancer is the most common malignancy in women. Incidence rate of breast cancer in Croatia is 119 cases per 100 000 and it is of great importance to identify additional prognostic factors that may have impact on survival.

The aim of this study was to determine prognostic value of lymphovascular invasion (LVI) in breast cancer patients with clinically node-negative axilla. Node-negative axilla is determined as absence of metastases in axillary lymph nodes detected by clinical examination or one of the imaging studies (excluding lymphoscintigraphy).

Retrospective analysis of medical history was conducted from January 2010 to April 2010 at University Hospital for Tumors. One hundred and sixty five patients with breast cancer were treated by surgery. Out of total number 114 patients were enrolled and fulfilled inclusion criteria (primary surgical treatment and clinically node-negative axilla). Statistical analysis was done. Fisher and Chi –square were used to determine correlation between LVI and histological/ clinical factors while Kaplan Meier test was used to determine connection between LVI and overall survival. Survival curves were compared using log-rank test. Value of $p < 0.05$ was statistically significant. Average age of patients at time of diagnosis was 59 years (range 34-85). Average tumor size was 2.2 cm (range 0.5-9cm). In 72 (63.2%) patients breast conserving surgery was done and 42 (36.8%) patients underwent total mastectomy. All patients underwent axillary staging. Postoperative, adjuvant chemotherapy was administered in 78 (68.4%) patients. The most common was anthracycline based regimen (74 out of 78 patients). Adjuvant irradiation was delivered in 88 (77.2%) patients, out of which 43 patients underwent only whole breast/chest wall irradiation, and in 45 patients additional regional nodal irradiation was delivered.

Five year survival was reached in 92.3% and median follow up was 79 months. Lymphovascular invasion was found in 15 (13.2%) patients. LVI was related with presence of perineural invasion ($p < 0.001$). Statistical analysis showed that LVI was not associated with tumor size, histologic grade, proliferation index Ki67 or with presence of axillary metastases. Moreover, association of LVI with overall survival or recurrence was not found ($p = 0.499$).

P17 – Mobile palliative teams and patient content with palliative care - experience from University hospital for tumors

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As oncologists, we are often confronted with hard decisions when it comes to our patients and treatment choices. At some point in cancer treatment we reach a stage when active treatment for our patients is not possible and we need to provide the best possible support in the terminal phase of their life. Palliative care is a medical discipline that offers medical and nursing care for people with life-limiting illness. It provides relief of patient's main symptoms which include pain, malnutrition, psychological stress and improves overall quality of life for patients and their families. In Croatia, there are Mobile palliative teams (MPT), including a doctor and a nurse, that provide care to terminal patients in their own home. Unfortunately, MPT aren't available in all parts of Croatia, and there are many patients who are not familiar with MPT.

Aim of this study was to assess the quality and accessibility of MPT.

We looked up all the patients that had attended our MDT in University Hospital for Tumors from May through August 2017, who were no longer candidates for active cancer treatment. We called them and asked several questions about their quality of life and palliative care. Some patients had died in the meantime. Finally, we were able to contact 52 patients willing to take part in this research.

41% of our patients were familiar with MPT. Only 18% of our patients were under the care of MPT regularly, 23% used it on occasion while 59% never used their services and care. There was a large difference between the population in cities, especially Zagreb, and other dislocated places. Only 27% of our patients rated their pain therapy as adequate, 59% rated their pain to be relatively under control but not completely, while 14% admitted their pain was not adequately managed. As far as psychological help, almost 80% of our patients have not received any psychological help, but majority of them have not even reached out for it.

Our research showed that awareness about palliative care is still inadequate and that our patients are not informed about MPT and the possibilities it provides. MPT are available to terminal patients and are better organized in cities than in rural areas. This research showed that we need to take better care of our patients at the end of their lives and allow them a more dignified and comfortable death.

P18 – Case report: Patient with HER2 positive breast cancer and luminal A metastases in the scalp

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In April 2016 a 58-year-old patient was diagnosed with ductal invasive breast cancer, HER2 positive, ER 93%, PR 92%, Ki67 16%, Luminal B. After further medical processing by skeleton scintigraphy multiple bone metastases were established, including the skull. In July 2016, in accordance with Croatian guidelines, 1st line treatment for the metastatic HER2 positive disease was initiated, including Perjeta, Herceptin and paklitaxel. After four cycles of therapy, in October 2016, control processing showed stationary disease and the same treatment protocol was continued. At the appointment for the continuation of treatment with the 7th therapy cycle in December 2016 the patient complained about itching in the scalp with alopecia areas. The treatment was paused and the patient was referred to a dermatologist. Biopsy of the lesions confirmed metastases of breast cancer in the skull. PHD: ER 80%, PR 90%, Ki67 8%, Luminal A. With regards to progression of the disease, the treatment was continued with hormonal letrozole therapy, which led to gradual complete regression of scalp changes, while control skeleton scintigraphy in August 2017 shows locations described earlier, only now their display is not as intense as before.

Skin metastases are quite frequent with breast cancer, but most frequently they occur on the thoracic wall. Metastases in the scalp were described, although they occur relatively rarely. Special caution is required with patients whose earlier anamnesis includes breast cancer or cancer that has been unknown so far because it can be the first manifestation of relapse, and in some cases the first manifestation of the disease.

P19 – Topics patients would like to confer about with an oncologist before the onset of systemic treatment

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Cancer diagnose in patients leads to various questions about illness itself, treatment possibilities and physical, psychological and social aspects of the illness. It is particullary important that the first conversation with an oncologist is as comprehensive and informative as possible for the patient as well as for the oncologist.

The aim of this paper is to identify topics that are of special interest to the patient in order to improve the quality of communication between patient and oncologist.

Questionnaire was designed based on a questionnaire for assessing the quality of life (EORTC QLQ-BR32). The questionnaire contains topics related to the illness and treatment, physical, psychological and social aspects of the illness. The questionnaire was completed by 35 women aged between 31 and 72, who began systematic treatment of early breast cancer in July and August 2017 at the University Hospital for Tumors, University Hospital Center Sestre Milosrdnice.

Topics that are of greatest interest for patients to confer about with an oncologist were related to the illness and treatment (median 5, IQR 1). All interviewed patients showed almost equal interest in topics related to physical and psychological aspects of illness (median 4, IQR 2). The smallest interest was about topics related to the social aspects of illness (median 3, IQR 2).

Almost equal interest for the topics was shown in all three age groups (30-44 years, 45-59 years, 60-75 years), with the greatest interest in topics related to the illness and treatment. The difference was that, in the age group 60-70 years, topics related to the psychological aspects of the illness were of greater interest than the topics related to physical aspects, as in the other two age groups.

By further systematic questionnaire implementation a more detailed insight into the personal wishes of the patient would be obtained and thus individualized approach to the patient and consequently improved patient's involvement.

P 20 – A case report: Occurrence of IgM mediated - autoimmune anemia after 1st application of taxane in neoadjuvant setting for hormone receptor positive, HER2 negative locally advanced breast cancer

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The term locally advanced breast cancer describes a disease confined to breast and regional lymph nodes by clinical, radiographic and laboratory findings. Standard therapy is preoperative anthracycline based chemotherapy followed by a taxane.

AIHA is caused by antibodies (AB) directed against red blood cell surface antigens. Autoantibody can be primary (idiopathic) or secondary (related to infection, immune disease or malignancy); can be „warm“ or „cold“, depending on the temperature by which antibodies are causing agglutination. Cold agglutinin disease (CAD) is rare and accounts for 15 % of all AIHA cases. In 90% of CAD cold agglutinins are IgM type, much rarely IgG and IgA type. Clinical significance lies in the fact that RBC lysis happens at temperatures lower than body core.

Patient aged 37; mother of two sons, aged 4 and 2, with no comorbidities was diagnosed with invasive locally advanced breast cancer shortly after lactation cessation. According to radiographic findings a tumor in breast was multicentric, axillary lymph nodes positive and according to MSCT there were no certain signs of metastatic disease.

Core needle biopsy showed invasive breast cancer (NOS) with neuroendocrine components; hormone receptor positive, HER 2 negative disease with high proliferation index (Ki67 \geq 90%).

She received 4 cycles of dose-dense-AC with gCSF support during which changes in RBC and WBC are as expected concerning the chemo-cycle phase. By the time of 4th cycle remaining tumor mass was minimal and axillary lymph node is not palpable any more.

Weekly paclitaxel (80mg/m²) was administered after a standard premedication. One week after a laboratory study revealed a 30% drop in Hb level and a significant rise in Pt number. No signs of hemorrhage nor lysis, no signs of inflammation, acrocyanosis, no pain in limbs or sign of tumor enlargement were present at that time. Direct Coombs test was positive (+++), antibody type IgM as well as presence of complement was proved. No changes in retinal blood vessels were noted as well as no organomegaly. Bone marrow was found hyper-cellular with no abnormalities in any cell line. Serial biochemistry test results did not reveal any signs of lysis nor elevation in inflammatory mediators. The relation of AB and taxane is yet to be clarified; there are no elements in favor of other secondary event. Staging and immunohematology testing are still in process by the time of completion of this case report...This is a case report of a patient treated preoperatively with an anthracycline based chemotherapy followed by a taxane who developed an autoimmune anemia after 1st taxane application.

P 21 – Osimertinib in the treatment of patients with T790M mutation

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Epidermal growth factor tyrosine kinase inhibitors (EGFR-TKIs) are used in patients diagnosed with lung adenocarcinoma with positive mutations in the epidermal growth factor receptor (EGFR). After progression on the first or second generation EGFR-TKIs (erlotinib, gefitinib, afatinib) 60% of patients acquire inhibitory T790M mutation. It is responsible for resistance to current therapy. In patients with T790M mutation, the third generation EGFR-TKI is indicated.

We administered osimertinib 80 mg once daily in 15 patients with advanced lung cancer who had radiologically documented disease progression after previous treatment with first and second-line EGFR tyrosine kinase inhibitors.

We treated 15 patients with osimertinib with stage IV lung adenocarcinoma. All patients were previously treated with first or second line EGFR TKIs (erlotinib, gefitinib or afatinib) and had radiologically documented disease progression. Four patients were males and eleven were females with median age of 60 years (ranging from 48 to 74). All patients were PS ECOG 0-1. Ten patients were never smokers, and five were ex-smokers. Two patients received osimertinib in second line setting, five patients in third line setting, 3 in fourth, 3 in fifth, one in seventh and one even in tenth line setting. 13 patients initially had deletion 19 in EGFR gene and two had L858R in exon 21 and then developed T790M mutation. In 13 patients T790M was proven from tumor tissue and in two patients by liquid biopsy. Median time to response was 5 weeks (ranging from 3 to 8). 10 patients had partial response (PR) and 5 patients had stable disease (SD). Progressive disease was observed in 3 patients after median treatment time of 12 months (2 to 18). Median duration of response at the moment is 6.5 months (ranging from 2 to 18). No significant side effects were observed.

Osimertinib is a highly effective drug in patients with proven T790M mutation after treatment with first or second generation EGFR-TKIs and it is crucial in further disease control. According to previously published studies, osimertinib has better efficacy and long-term disease control compared to chemotherapy.

P 22 – The Correlation between findings of preoperative MR and definitive PHD of the primary tumor after neoadjuvant treatment in breast cancer patients

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Neoadjuvant treatment (NAC) of breast cancer patients allows in vivo monitoring of tumor response to applied therapy, conserving surgical procedures, better patient quality of life, and better survival, if a pathologically complete response (pCR) to treatment is achieved.

The use of MR in assessment of response to NAC has shown in various studies a minimum of 70% sensitivity and specificity in the detection of residual disease, with high positive and negative predictive value. Studies have shown greater accuracy in predicting pCR in HER2 positive tumors and higher rates of false negative results in HER2 negative tumors.

In the period from 12/2013 to 8/2017 at the University Hospital for Tumors Zagreb, 155 patients with breast cancer were treated neoadjuvantly. We analyzed the correlation of findings of preoperative MR after NAC and definitive PHD after surgery, for primary tumor in the breast.

The analysis included 70 patients. Reasons for not - including the remaining number of neoadjuvantly treated patients into this analysis were as follows: NAC still undergoing or not fully performed, unavailable finding of MR or PHD, lost from follow - up, recorded progression of disease during NAC, death.

The median age of the analyzed patients was 55 years. The prevalence of the individual surrogate subtypes of the disease was as follows: HER2 tumor 21.4% (15/70), triple negative breast cancer 15.7% (11/70), luminal HER2 positive 18.6% (13/70) and luminal HER2 negative 44.3% (31/70).

According to MR of the primary tumor, the clinically complete response (CCR) to NAC was achieved in 51.4% (36/70) patients, and the finding of residual tumor was described in 48.6% (34/70) patients. Post-operatively, the PHD of the primary tumor in the breast showed pCR in 37% (26/70) patients, and the remaining disease in 63% (44/70) cases. The overall correlation between MR and PHD is 72% in the assessment of complete response, and 77% in the estimate of residual disease.

Analyzed by subgroups, the results are as follows: in the HER2 tumor group, the correlation between MR and PHD in the assessment of complete response was 92% and in the estimate of residual disease 75%; in the group with triple negative breast cancer the correlation between MR and PHD in complete response was 80% and residual disease 86%; in the luminal HER2 positive tumor group the MR and PHD correlation in complete response, as well as in the residual disease was 100%, while in the group with luminal HER2 negative tumor the correlation between MR and PHD in the assessment of complete response was 28.5%, and for the residual disease 63%.

The results of our analysis showed a high total matching of MR and PHD, which is consistent with the results of world studies and confirms MR as a good method for monitoring response to NAC. Subgroup analysis distinguishes patients with luminal HER2 negative tumor. In this group, the achievement of the complete response to NAC is the smallest, as well as is the lowest correlation between MR and PHD findings. This confirms the known weaker response of this type of tumor to neoadjuvant treatment, but also points to the need for additional caution when analyzing MR findings in these patients.

P23 – Evaluation of *burn-out* syndrome in oncology employees

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Burn-out syndrome is a state of mental, physical or psychophysical exhaustion caused by prolonged and intensive stress. Among the all oncology clinics, medical oncology have the highest born-out syndrome, according to literature sources. Thus, we analyzed prevalence of burn-out syndrome, its intensity and main characteristics, by oncology employees in Clinical Hospital Center Zagreb. We evaluated different parameters like age, sex, level of education and duration of internship. There were 111 examinees, out of them 67 nurses and 44 medical doctors. According to age, dominantly it was younger population, with about 68% of them under 40 years. All examinees had to fulfill *Maslach burn-out inventory*, which was licensed and designed to measure 3 categories of burn-out syndrome - emotional-exhaustion (EE), depersonalization (DP) and personal-accomplishment (PA). This research was obtained during the year 2017. For statistical analysis has been carried out using descriptive statistics, Pearson correlation, non-parametric statistical analyses like Kruskal Wallis and Mann Whitney tests. We concluded that there is a strong statistical correlation between emotional exhaustion and depersonalization regarding the age of participants. It is interesting that it was more pronounced in males. We also found positive correlation between emotional exhaustion and depersonalization and age of participants. The strongest evidence we found in range between 41 and 50 years, and above 60. Profession profile seems to be important as well (doctors more exposed than nurses) and consequently the level of education as a parameter. Majority of these results confirm data in literature, but we found some specific features, probably intrinsic for our hospital, usually not described in other reports.

P 24 – Analysis of circulating leptin in breast cancer patients

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Leptin is an adipokine that is involved in regulation of energy balance in the body. Leptin affects different processes during growth and metastasis of solid tumors: cell proliferation, angiogenesis and tumor invasion. The interaction between leptin and cytokines in breast cancer has been shown. Furthermore, leptin signaling has been implicated in cancer chemoresistance.

The aim of this study was to determine the concentration of leptin in breast cancer patients and compare it to the values in healthy controls.

The study included serum of 169 breast cancer patients and serum of 20 healthy controls. Serum leptin concentration was determined by ELISA (Enzyme-linked Immunosorbent Assay). The cut-off value was determined by ROC (receiver operator characteristic) analysis.

According to the ROC analysis the cut-off value of leptin in serum was 3.03 ng / ml. In 88 patients leptin serum values were more than 3.03 ng / mL (3.5-9.71, mean value 5.78) and in 81 patients the values were below 3.03 ng / mL (0-1.6, mean value 0.58). Sixteen healthy subjects had leptin values below the cut-off value (0.02-3.03: mean 1.25), and 4 subjects had higher values (3.11-3.23; mean value 3.17). Serum leptin concentrations in breast carcinoma patients were statistically significantly higher than those in healthy individuals. We found a statistically significant correlation between the age of the patients and the serum leptin concentration. Leptin serum values of women under the age of 50 were higher than the leptin serum values of women over 50 years of age.

Our results suggest higher values of circulating leptin in breast cancer patients compared to healthy individuals.

P 25 - Influence of upper-body function on the quality of life in patients treated with adjuvant systemic antineoplastic treatment at the University Hospital for Tumors

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Breast cancer survival rates are today much higher in comparison with different cancer sites, resulting in an increasing number of women who survived breast cancer (cancer survivors). It opens the door to a new issue of their quality of life, which represents an important personal and public health problem. The articles published on this topic demonstrated that between 15 and 45% surviving breast cancer patients had a diminished function of the upper extremity (upper body function /UBF) due to lymphedema, up to one year after the performed surgical treatment. Most published literature describing UBF associated with breast cancer compares the outcome regarding to various methods of breast cancer treatment (sentinel lymph node biopsy versus axillary dissection, breast sparing surgery versus mastectomy, chest and axillary radiation versus only axillary radiation) and it is often limited by the use of various methods in measuring the upper-body function, usually without an adequate clinical evaluation. There is a lack of literature on the effect of lymphedema on the quality of life of breast cancer survivors and on the benefit of early evaluation and treatment.

This study describes the effect of the upper extremity function on the quality of life of patients with less than 70 years of age, with the diagnosis of invasive unilateral breast cancer, treated with adjuvant systemic antineoplastic treatment at the University Hospital for Tumors. Data were collected through a valid DASH questionnaire (DASH -disability of the arm, shoulder and hand), an instrument which consists of a 30 symptoms scale, ranging from 0 to 100, where 0 represents the absence of any difficulty, and 100 represents significantly impaired function of upper extremity. Significant negative impact on the quality of life of the patient was considered DASH score > 25. The questionnaire also detected changes in expression of difficulties over time, with the change of 10 and more points considered as significant (minimal important change).

The patients filled out the questionnaire themselves at the beginning of the adjuvant treatment (within 1 month after the performed surgery) and at the end of the adjuvant treatment (6 months after the performed surgery) and their responses were compared to determine the effect of the upper extremity function on the patient's quality of life and for comparison of responses depending on time past from operative treatment.

Results: 62 patients participated in the study. DASH score higher than 25 at the beginning of adjuvant treatment had 34 (54.8%) patients and at the end of adjuvant treatment 21 (33.8%) patients. The average DASH score at the beginning of adjuvant treatment was 35 (median 22) and at the end of adjuvant treatment 24 (median 23). In 42 (67.8%) patients there was a change in DASH score and the biggest change was 19.

Conclusion: The DASH questionnaire can detect and distinguish minor and significant changes in the function of the upper extremity in patients with lymphedema. At the beginning of adjuvant treatment, a significantly greater number of patients cited difficulties in daily activities resulting in a disturbed upper extremity function, which negatively reflected on their quality of life. Early assessment and early physiotherapy treatment can significantly improve their functioning. The study refers to the important role of early clinical evaluation and treatment of lymphoedema in breast cancer patients. Further prospective studies are needed to adequately address this problem.

AUTHOR INDEX

B

Badžek, I. 22, 26, 27
 Bajić, Ž. 22
 Bašić Koretić, M. 33
 Belac-Lovasić, I. 38
 Belev, B. 10, 43, 44
 Bilić, I. 44
 Bilić Knežević, S. 37
 Bilobrk, J. 25
 Bitar, L. 41
 Bošnjak, M. 34
 Brkić, I. 24
 Budimir, B. 21, 30
 Budisavljević, A. 15
 Bukovica, A. 38

Č

Čonkaš, M. 5

Ć

Ćuk, B. 21, 25, 30, 31

D

Dedić Plavetić, N. 13, 25,
 33, 44
 Demser, M. 43
 Dmitrović, B. 12
 Dobrila Dintinjana, R. 9
 Drpa, G. 21, 30

G

Gnjidić, M. 8
 Golem, H. 32
 Goršić, I. 32
 Grubišić-Čabo, F. 34
 Grubišić-Čabo, R. 34

H

Herceg, D. 33

J

Jakić-Razumović, J. 25
 Jakopović, M. 21, 41
 Ječmenica, D. 29
 Jurčić, P. 23

K

Kamenečki, V. 45
 Kardum Fučak, I. 40
 Kekez, D. 32
 Kolarić, V. 29
 Koršić, M. 41
 Kovač, M. 39
 Kovač, Z. 44
 Križić, M. 33
 Krpina, K. 21, 30, 41
 Krstić, C. 28, 37
 Kukulj, S. 21, 30, 41
 Kulić, A. 11, 33, 44
 Kurbel, S. 7, 12

L

Ladenhauser, T. 14
 Lampalo, M. 21
 Librenjak, N. 32
 Lonjak, N. 22, 26, 27, 28, 36, 37,
 42, 45

M

Maloševac, S. 24, 31
 Mandić, S. 25, 31
 Mihaljević, S. 7
 Miletić, M. 37
 Mojsović, A. 34

N

Nalbani, M. 35
 Nikles, I. 22, 26, 27,
 36, 37
 Nikles, S. 36

P

Pacić-Hardi, N. 31
 Paić, M. 34
 Pavlović, M. 16, 22, 42
 Pleština, S. 32, 41
 Podolski, P. 33
 Popek, I. 24
 Prejac, J. 17, 32

R

Radić, P. 25
 Radmilović Varga, Lj. 29, 33
 Raguz, J. 22, 26, 27, 28, 36, 37
 Redžović, A. 9
 Reljić, D. 34

S

Samaržija, M. 21, 41
 Sedlić, F. 44
 Seiwerth, F. 41
 Silovski, T. 3, 6
 Simetić, L. 35
 Sirotković-Skerlev, M. 44
 Skočilić, I. 38

Š

Šahbazović, A. 28, 37
 Šeparović, R. 4, 22, 24, 26, 27,
 28, 36, 37, 42, 45

T

Tečić Vuger, A. 4, 22, 42, 45
 Tolj, I. 25
 Tomljanović, I. 38

V

Veliki Dalić, I. 36
 Vidović, M. 32
 Vrbanec, D. 25, 33, 44
 Vrbanec, J. 18
 Vuković, P. 22, 26, 27, 28, 36,
 37, 42

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Massad L S, Halperin C J, Biterman P. Correlation between colposcopically directed biopsy and cervical loop excision. *Gynecol Oncol*. 1996;60:400-3.

Book chapters

Melter PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. *The genetic basis of human cancer*. New York: McGraw-Hill; 2002. p. 93-113.

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