POSTERS

P1 - Acquired rhinophyma as a paraneoplastic manifestation of non-small cell lung cancer

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We report a case of a 58-year-old man who developed rhinophyma caused by non-small cell lung cancer.

This paraneoplastic manifestation was set because of chronological coincidence between the disappearance of the rhynophyma and chemoradiotherapy and the appearances of rhinophyma and the progression of the disease.

The patient is a 58-year-old male who was treated for diabetes, when he developed rosacea for which he was unsuccessfully treated with antibiotic therapy. He was admitted to our hospital, due to chest pain persisting for 55 days, fever up to 37.4 C, fatigue and 7 kg weight loss. On chest radiography was found irregular infiltrate with central collapse on right upper lobus and thickening of apical pleura. Follow-up computed tomography imaging confirmed the presence of a consolidation infiltration while follow-up cytological analysis of material gained by catheter aspiration revealed carcinoma (poorly preserved squamous cells). Due to the advanced stage of the disease (stage IIIA), patient was treated both with chemotherapy (4 cycles of neoadjuvant therapy (gemcitabine and cisplatin)) and radiotherapy. During chemoradiotherapy the withdrawal of rhinophyma has occurred and computed tomography imaging showed regression of the disease from stage IIIA to stage IIB, for which patient soon underwent right thoracotomy with upper lobectomy and radical lymph node dissection. Two months after surgery, patient experienced re-emergence of rhinophyma followed by increased tumor markers (CYFRA 21-1 was 4.5) for which he received second-line chemotherapy (4 cycles of paclitaxel and carboplatin). After 2nd cycle of chemotherapy rhinophyma has again withdrawn and the patient experienced remission of the disease. Two month after chemotherapy subsequent whole body F18- FDG positron emission tomography (PET) was performed and documented metastasis on right lung, second and third rib and suprarenal gland. The patient received erlotinib therapy after which once again experienced remission of rhinophyma for a brief time (one month), since he due to progression of carcinoma passed away shortly thereafter.

P2 - *UGT1A1*28* polymorphism and toxicity of FOLFIRI protocol – a single-institution cohort

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Treatment with irinotecan in combination with infusional 5-FU, is still one of the pillars of oncologic approach to patients with metastatic colorectal cancer. Unfortunately, toxic collateral damage to normal tissues produces many side-effects of the drugs. UDP-glucuronyl transferase (UGT1A1) is the rate-limiting enzyme of the irinotecan metabolism, responsible for bulk degradation of injected compound (up to 80%). Fluoropyrimidines are to similar extent inactivated by dihydropyrimidine- dehydrogenase (DPD). Genes for these two metabolic enzymes can harbor pathogenic polymorphisms resulting in partial or complete enzyme-deficiency leading to disturbed pharmacokinetics as well as increased risk for toxicity. Pharmacogenetic testing may give valuable information for individualization of therapy as deficiency can be detected by *UGT1A1* and *DPYD* genotyping. Most common UGT1A1 variant among Caucasians is *UGT1A1*28*, resulting in Gilbert's syndrome among homozygotes, with significantly increased risk for irinotecan-induced side effects. Whether heterozygotes for *UGT1A1*28* also have diminished tolerability of irinotecan requiring dose-reduction is still a matter of debate. We have found scarce published data on prevalence of *UGT1A1*28* polymorphisms among oncologic patients of Croatian descent. *DPYD*-locus may be affected by few dozens of variants with uncertain functional relevance. No significant data was published on genetic background considering *DPYD* among patients of this geographic region. Here we present the preliminary results of a single-institution patient cohort genotyped for *UGT1A1*28* and some major *DPYD* variants and followed-up for toxicity during irinotecan/5-FU therapy (FOLFIRI-protocol).

FOLFIRI-treated patients (N=114) were genotyped for *UGT1A1*28* as well as for five major *DPYD*-polymorphisms (**2A*, **13*, *c.2846A>T*, *c.1236G>A* and *c.496A>G*). Adverse events were monitored for three months from the beginning of treatment. Observed group included grade III and IV toxicity (N=52), whereas control group comprised grade I and II (N=62). DNA was isolated from whole blood (3ml) and genotyped according to manufacturer's propositions using real-time PCR (LightCycler® for *UGT1A1*, TaqMan® for *DPYD*). Frequencies of the polymorphisms were tested by non-parametric statistical tests and binary logistic regression.

A total of 206 adverse events were recorded during observation period (75 of high and 131 of low grade). Subjects in observed group (toxicity grade III and IV) developed adverse effects more rapidly and accumulated greater total number of events *per capita*. *UGT1A1*28* polymorphism was detected in 58% of tested subjects. Both homozygotes and heterozygotes were at significantly increased risk for toxicity (OR=20.58 and 5.47 respectively). Aggregated *DPYD* polymorphisms (N=33; 28.9%) distributed unevenly with higher frequency of carriers in observed group (38.46% vs. 20.97%), thus creating a statistically significant increase of risk for severe toxicity among carriers of mutated *DPYD* variant (OR=2.36). *UGT1A1*28* variant had stronger influence on toxicity-risk than *DPYD* polymorphisms considering patients given irinotecan in combination with 5-FU, as expected form literature.

Significant association and predictive value of *UGT1A1*28* polymorphism among patient given FOLFIRI-protocol is shown, while mutation status of *DPYD* has shown weaker but still significant influence. Frequencies of detected polymorphisms were in slight discordance considering data from literature, thus emphasizing importance of genetic background among different genotyped ethnic groups.

P3 - Preclinical evidence on the anticancer properties of phytocannabinoids

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Phytocannabinoids are unique terpenophenolic compounds predominantly produced in the glandular trichomes of the cannabis plant (*Cannabis sativa* L.). The delta-9 tetrahydrocannabinol (THC) is the main active constituent responsible for the plant's psychoactive effect and, together with the non-psychoactive cannabidiol (CBD), the most investigated naturally occurring cannabinoid. The first report on the antitumor properties of cannabis compounds appeared more than forty years ago, but the potential of targeting the endocannabinoid system in cancer has recently attracted increasing interest.

Our study aimed to review the last decade's findings on the anticancer potential of plant-derived cannabinoids and the possible mechanisms of their activity.

A large body of *in vitro* data has been accumulated demonstrating that phytocannabinoids affect a wide spectrum of tumor cells, including gliomas, neuroblastomas, hepatocarcinoma as well as skin, prostate, breast, cervical, colon, pancreatic, lung and hematological cancer. It has been found that they can stop the uncontrolled growth of cancer cells through the cell-cycle arrest, inhibition of cell proliferation and induction of autophagy and apoptosis. They can also block all the steps of tumor progression, including tumor cell migration, adhesion and invasion as well as angiogenesis. The observed effects are mainly mediated by the cannabinoid CB1 and/or CB2 receptors, although some other receptors and mechanisms unrelated to receptor stimulation may also be involved. The majority of available animal studies confirmed that phytocannabinoids are capable of effectively decreasing cancer growth and metastasis *in vivo*. THC was found to be effective against experimental glioma, liver, pancreatic, breast and lung cancer while CBD showed activity against glioma and neuroblastoma, melanoma, colon, breast, prostate and lung cancer. Further *in vitro* and *in vivo* studies also greatly support their use in combination with traditional chemotherapy or radiotherapy, which results in improved efficiency, attenuated toxicity or reduced drug resistance. Taken together most of available preclinical results emphasize the extensive therapeutic potential of THC and CBD in various types of cancers. The potential clinical interest of cannabinoids is additionally suggested by their selectivity for tumor cells as well as their good tolerance and the absence of normal tissue toxicity, which are still the major limitations of most conventional drugs. The accumulated preclinical evidence strongly suggests the need for clinical testing of cannabinoids in cancer patients.

P4 - Colon carcinoma with a metastasis into breast, a case study

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In August, 2009, a 55-year-old female patient visited her doctor because of abdominal pain. Endoscopy verified a malignant process of the ascendental colon whose PHD corresponded to adenocarcinoma. Right-side hemicollectomy with ileotransversal anastomosis was done; regarding the third stage of the illness, in further treatment adjuvant chemotherapy was carried out in 6 cycles – 5FU/LV.

After 2 years a control evaluation showed a relapse on the anastomosis and multiple metastases on the lungs. A resection of the local relapse was done after which the patient was treated with chemotherapy through combined protocol based on irinotecan with a good response and regression of the number and size of the pulmonal metastases. Then a thoracotomy with radical metastasectomy of the two remaining metastases of the right lower lobe. In June 2013, a control PET-CT test again shoved a suspected local relapse of the illness so that a repeated surgery was indicated. Intraoperative findings confirmed a relapse on the anastomosis, so a resection of the transversal colon and terminal ileum was done. In the postoperative period the patient underwent 3 chemotherapy cycles according to CapeOx protocol after which the control evaluation did not show any clear signs of the illness activity.

In March 2015, owing to severe abdominal pain and a suspected illness relapse there was a repeated surgery. Intraoperatively a tumor size 18 cm was verified having originated in the left ovary which had spontaneously ruptured with metastases in the small intestines and sigmoid colon. A surgery of sigmoid colon resection according to Hartmann was done, also a resection of the metastases on the small intestines, hysterectomy with adnexectomy on both sides and extirpation of the tumor on the left ovary. PHD finding confirmed metastatic adenocarcinoma, so the patient was consequently treated with chemotherapy according to FOLFOX IV protocol. After 5 cycles a control PET-CT was done which showed a metabolically active node in the right breast, without any signs of active illness in other parts of the body. A carcinoma was cytologically confirmed so in November 2015 a tumor extirpation was done.

Immunohistochemical analysis proved a secondary process, ER neg, PR neg, HER-2 neg, Ki67 70% with present expression CEA, CK20, CDX2 neg. 2 months later the patient was hospitalized with a clinical picture of obstructive ileus. Intraoperatively an inoperable solid malignant block with inset bowel folds – from the surgical point of view an incurable condition. Regarding the surgical findings and a deterioration of the general condition a confirmed active oncological treatment was given up and palliative care was indicated.

Metastases into a breast of other primary tumors are rare consuming only about 2% of all breast metastases. Lymphomas, metastatic melanoma and bronchi carcinoma are those that account for the majority of breast metastases.

Breast metastases of the colorectal carcinoma have been described in literature in very few cases and point to an expansive and agressive illness where surgical treatment and a systemic oncological treatment have a very limited role.

P5 - The use of Edmonton Symptom Assessment System (ESAS) in patients with metastatic melanoma at the time of admission to Medical Oncology Clinic (MOC), Institute for Oncology and Radiology of Serbia (IORS)

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ESAS has been proposed as a symptom screening tool in cancer patients. It consists of numerical rating scales (0-10) for self-assessment of eight most common cancer-related symptoms as well as patient's well-being, with a 10th scale for a patient-specific symptoms. The goal of this study was to examine the use od ESAS as an inital symptom screening tool in patients with metastatic melanoma at the time of admission to MOC, IORS.

During a four week study period, patients with metastatic melanoma assessed disease-related symptoms using an ESAS at the time of admission. Descriptive statistics methods were used to analyze collected data.

Symptoms were assessed in 12 patients (7 male and 5 female). Median age was 63 years (range 35-80) with median performance status (PS) of 1 (range 0-3). All nine ESAS symptoms were reported as less than 4 by majority of patients with mean scores of 1.73, 0.70, 1.61, 0.57, 2.03, 1.53, 1.03, 1.18 and 2.06 for pain, nausea, loss of appetite, shortness of breath, fatigue, depression, drowsiness, anxiety and well-being, respectively.

This study has shown that the ESAS is practical and not time-consuming tool for initial assessment of cancer-related symptoms in patients with metastatic melanoma at the time of admission at the MOC, IORS. Further research will be conducted in order to examine the role of ESAS in assessment of symptom burden in these patients and its impact on treatment decision-making process.

P6 - Influence of molecular subtypes of metastatic breast cancer on clinical manifestations and disease outcome

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The breast cancer is the third cause of cancer-related mortality in Europe, after lung and colorectal cancers. According to Ferlay et al. breast cancer incidence in Montenegro is 75.9/100.000, while mortality rate is 27.6/100.000. In Montenegro, breast cancer is not just the most frequent cancer in women, but also the first cause of cancer related death.

Aims of this study were establishing metastatic breast cancer molecular subtypes distribution, correlation between metastasis patern and molecular subtype, as well as correlation between molecular subtype and clinical parameters.

The research was conducted on a sample of 214 women, who were diagnosed with breast cancer relapse in form of distant metastasis in time 6 years long time period (2006 till end of 2012). Minimal follow up period was 24 months, till the end of year 2014.

Every patient was classified into one of four groups, with usage of available immunohistochemical approximation: 1. Luminal A like (Er+, Pr+, HER 2 0); 2. Luminal B like (Er+, Pr+/-, HER 2 +); 3.HER 2 (Er-, Pr-, HER 2 +); 4.Triple negative (Er-, Pr-, HER 2 0).

Median age at metastatic disease diagnosis was 58.2 years. Out of total number of patients, 56% had the luminal A molecular subtype, 18% had the HER2 subtype, 16% had the triple negative subtype, while the least frequent, at only 10%, was the luminal B molecular subtype. The patients with HER2 subtype developed brain metastasis more frequently than those with the other subtypes ($p=0.023$). The patients with luminal subtypes A and B more frequently developed bone metastasis, as the first and the second site of relapse ($p<0.001$). Patients with HER2 and triple negative subtype had more frequently paliative radiotherapy as treatment ($p<0,001$).

The patients with the HER2 and triple negative subtypes had shorter cumulative survival comparing to those with luminal subtypes ($p=0.011$). Median time to progression was 15 months. According to our results, time to progression in patients with the HER2 and triple negative subtypes was shorter than average ($p=0.027$), respectively 11.6 and 12.4 months. At point of two years follow up, only 35% of HER2 subtype patients and 40% of patients with the triple negative subtype were alive, in contrast with the significantly larger proportion of patients with the luminal subtypes. Metastatic sites, time to progression and survival varied by subtype as approximated by ER, PR and HER2. The HER2 subtype was a predictor of worse outcomes and poor survival.

P7 - The efficacy and tolerability of slow-release (SR) hydromorphone in the treatment of cancer dyspnea in lung cancer patients: experience from the Institute for oncology and radiology of Serbia (IORS)

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Cancer related dyspnea and pain are common in patients with lung cancer. Morphine is an effective medication for both symptoms. Oral SR morphine is not available in Serbia. Oral SR hydromorphone is used instead. The efficacy and tolerability of immediate-release (IR) hydromorphone in the treatment of cancer dyspnea was documented in the literature.

Objective of our study was to assess the efficacy and tolerability of oral SR hydromorphone (24h release) for the treatment of cancer pain and dyspnea in lung cancer patients.

Twenty five patients with lung cancer with severe dyspnea and pain (both assessed on 0-10 numeric rating scale) were included. On day 1 (D1) patients were treated with oral IR morphine 5 mg Q4h with the same dose for the breakthrough pain and dyspnea. In all patients who required at least 30 mg of oral IR morphine for 24 hours period, SR hydromorphone 8 mg were included in the treatment on day 2 (D2) with IR morphine 5 mg forforthe breakthrough pain and dyspnea. On D2-D5 the efficacy and tolerability of SR hydromorphone as well as adverse effects were monitored.

On D1, the mean intensity of dyspnea was 7.48(SD=0.510). On D5 all patients were still on 8 mg of SR hydromorphone without the need of morphine for the breaktrough pain or dyspnea. On D5 the mean intensity of dyspnea was 2.48(SD=0.770), with significantly less intensity compared to D1 ($p<0.001$). There were no registered side effects of SRhydromorphone.

Use of convenient SR hydromorphone resulted in sustained relief of dyspnea as well as pain with acceptable tolerability.

P8 - Metastatic renal cell carcinoma: First-line treatment choice in everyday practice – personal experience

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Over the past decade marked advances in treatment of metastatic renal cell carcinoma (mRCC) have been made, with targeted agents that inhibit vascular endothelial growth factor and its receptor (VEGF, VEGFR) or mammalian target of rapamycin complex (mTOR). Standard therapies for first-line treatment of metastatic good and intermediate risk clear-cell renal cell carcinoma are sunitinib and pazopanib also approved by Croatian Institute for Health Insurance. COMPARZ study has demonstrated that both drugs have similar efficacy but different side-effect profiles. There are no recommendations or predictive biomarkers to help in choosing between them and the choice is mainly based on clinical parameters. Besides, patients in routine clinical practice are not similar to those enrolled into clinical trials. When high-level evidence is not available for treatment decisions, personal experience or medical community might provide guidance.

We performed this retrospective comparative analysis of mRCC patients treated between 2014 to 2016 at our insitution in order to try to identify parameters influencing the choice between the two drugs. Fourteen patients recieved sunitinib and 19 pazopanib. We analysed following parameters: sex, age, place of residence, MSKCC risk group, number of metastatic sites, prior nephrectomy, tumor grading, number of comorbidities. We also analysed progression-free survival (PFS) and overal survival (OS).

The two groups did not differ significantly according to sex, age, place of residence, number od metastatic sites and prior nephrectomy. There was a trend towards prescribing sunitinib more frequently to patients with more aggressive disease (higher MSKCC risk group and tumor grade) but the difference was not statistically significant. Patients with two and more comorbidities more frequently received pazopanib (p=0.036). No differences in PFS and OS between the groups were noted.

We prescribed pazopanib more frequently to patients with comorbidities and had a slight tendency to prefer sunitinib in patients with high-risk tumors. There were no differences in survival outcomes between the two groups. These results are consistent with known large real-life studies.

P9 - When to stop the treatment of venous thromboembolism in cancer patients

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Despite adequate anticoagulation treatment cancer patients who gets venous thromboembolic (VTE) complication have, comparing to general population, higher incidence of rethrombosis, but also of bleeding. It is generally accepted that these patients should be treated with anticoagulations for 3-6 months. Such an attitude is a consequence of 3 randomised trials, in this field, in which the patients have been treated for 3 months, as well as the fact that in the largest study they have been treated for 6 months. As a consequence of absence of trials, which would resolve the problem of continuation or withdrawl of the therapy after 3-6 months of treatment, we make our decisons based on estimation of the value/risk of continuation anticoagulation treatment, regarding the risk of rethrombosis, risk of bleeding; tolarebility of the treatment; patients choice as well as the acitivity of malignant tumor.

P10 - Malignancy-related ascites; clinical significance and impact on prognosis

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The appearance of malignancy-related ascites usually heralds the onset of advanced disease and portends a poor prognosis. We conducted a retrospective study of 43 patients who underwent therapeutic abdominal paracentesis for malignancy-related ascites between October 1st, 2015 and March 31st, 2016 at our institution. The population included 23 males and 20 females with a mean age of 64 years (range, 22-81 years) diagnosed with metastatic disease, the most common of which included gastrointestinal cancer (28 patients) and ovarian cancer (7 patients). The sites of metastases at diagnosis of the ascites as demonstrated by diagnostic imaging techniques included liver (19 patients), lymph nodes (18 patients), peritoneum (13 patients), lung and pleura (5 patients), bones (3 patients), and rare metastatic sites (3 patients). The most frequent symptoms of the malignancy-related ascites were abdominal distension (90.7%), shortness of breath (34.9%), abdominal discomfort or pain (16.3%), leg swelling (16.3%), vomiting (11.6%), nausea (9.3%), constipation (4.7%) and general weakness (4.7%). The mean volume drained by paracentesis was 4000 milliliters per procedure (range, 1200 milliliters to 6000 milliliters). Diuretics were used in 30 patients with furosemide used in 29 (67.4%), spironolactone in 18 (41.9%) and combination of both in 17 (39.5%). None of the patients in this series had either continuous peritoneal ports or catheters drainage. The patients with gastrointestinal cancer had higher values of serum urea (13.6 mmol/L) than other (7.4 mmol/L) (p=0.0323). The values of serum urea in the patients with gastrointestinal cancer were also greater than in the patients with ovarian cancer (6.9 mmol/L) (p=0.0392). The patients with liver metastases on average were older (72 years) than the other patients (63 years) (p=0.0169), and had higher values of serum bilirubin (36.4 μmol/L) than other (10.6 μmol/L) (p=0.0292) as well. The patients with nausea had higher values of serum urea (20.15 mmol/L) than the other (7.8 mmol/L) (p=0.0384). The patients presented with swollen legs had significantly lower INR than the other (p=0.0365). The survival period after the patients were diagnosed with ascites was between 2 and 339 days (the median value was 24 days). The patients with ovarian cancer had the average survival period of 93 days (between 5 and 339 days). The patients with gastrointestinal cancer had an average survival period of 35 days (between 2 and 201 days). Regarding the primary cancer diagnosis, the survival analysis showed a statistically significant difference in the dynamics of mortality (p=0.0352). Three patients with ovarian cancer died within 20 days, and the other four lived for about a year. Nearly all patients with gastrointestinal cancer died within three months. After abdominal paracentesis, the patients with liver metastases lived for 19 days on average (3 to 149 days), while the patients without liver metastases lived for 86 days on average (2 to 339 days) (p=0.0120).

P11 - Efficacy and safety of antivascular drug after anti-EGFR; aflibercept after panitumumab, a clinical case

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A 40-year-old male with a negative family history of cancer and longstanding extensive ulcerative colitis, who was treated with mesalazine, was referred in July 2016 for a regular follow-up colonoscopy. A stenotic cancer in the hepatic flexure was detected with the histological finding of poorly differentiated adenocarcinoma. Comprehensive whole-body imaging revealed the multiple bilobar liver metastases and the absence of pulmonary and bone metastases. The patient underwent right hemicolectomy. The definitive pathological investigation confirmed the previous histological findings, pT4a (focal perforation of serosa) R0 pN2 [4/56] pM1[hep] pL1, pV1, pPn0, G3, wild-type RAS. The perioperative upper-extremity deep venous thrombosis was treated as a paraneoplastic feature. The patient was assigned to mFOLFOX6 and panitumumab as the first-line treatment protocol. During this treatment, the patient developed papulopustular rash of the face and the trunk grade 2 NCI-CTCAE v.4.0. Additional mutation screening revealed the presence of PIK3CA mutation in exon 9 (E542K) and the absence of BRAF mutations in primary cancer and lymph node metastases. A daily 100 mg dose of acetylsalicylic acid was added to standard therapy. After four cycles, the increment of serum markers (CEA, CA19-9) was noticed. Computed tomography scan of the abdomen revealed progression in size of liver metastases. Due to liver-limited disease, the multidisciplinary tumor board did not exclude the possibility of resection. Consequently, FOLFIRI and aflibercept were introduced in January 2017. After two cycles, the serum markers were in significant decrease. After four cycles, the values of serum markers were halved. The abdominal computed tomography scan findings suggested a constant size of liver metastases but with central necrosis. Due to the omitted unacceptable gastrointestinal toxicity, it was decided to continue with the same line for the next four cycles. After the fifth cycle, the asymptomatic arterial hypertension second-degree NCI-CTCAE v.4.0 occurred. Nevertheless, it was kept under control with antihypertensive. The next appointment for diagnostic imaging and laboratory test is scheduled for May 2017.

P12 - Long–term chemiosensitivity of epithelial ovarian cancer: case report

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The significance of ovarian cancer is disproportionaly larger than its frequency, because, although it counts less than a quarter of gynecological malignancies, it is a cause of mortality of half of the women with gynecological cancer. Epithelial ovarian cancer is the most common type of cancer and most of EOC are diagnosed in advanced stage.

Although it is a highly sensitive tumour, with accomplishment of significant percentage of remission on first chemoherapy , about 75% of women relapse in the first three years. The standard treatment of reccurent EOC is successive apply of several therapy lines, and secondary citoreduction is indicated in selected cases.

Specific treatment of epithelial ovarian cancer of initial stage IIIA, at our patient, started in 2007, with total hysterectomy with billateral adnexectomy and omentectomy. In NED stage of the disease, postoperative therapy with paclitaxel - carbopatine was conducted.

Two years after, in the first relapse, patient received four cycles of ChT Taxol-CBDCA. Further use of this protocol was stopped because of allergic reaction to carboplatine.

Treatment was continued with weekly paclitaxel, and after the second cycle, disease progression was registered, and the secondary ChT regimen PAC was introduced. Five cycles of secondary ChT were administered, with the effect of CR.

In July 2012, PD was verified, and nine cycles of gemcitabine with bevacizumab were administered with the effect of PR. Considering effect and hematological toxicity, maintenance therapy with bevacizumab was continued. Thirteen cycles were applied, with the effect PD, so salvage chemotherapy weekly paclitaxel – cisplatine started.

After the fourth cycle, PR was declared ,but, due to peripheral sensory neuropathy grade 3, chemotherapy was suspended. Pregabaline was induced as neurological toxicity therapy, which led to recovery to the grade which made possible repeated use of cisplatine.

Six months after, disease progressed, when Taxol-CDDP was rechallanged. After the fourth cycle evaluation showed PR, but due to deterioration of peripheral neuropathy to grade 3, citostatic therapy was withdrawn.

In August 2015, PD was verified, so, with recovery of peripheral sensory neuropathy to grade 2, sensitivity to cisplatine, cummulative dosage of doxorubicine, five cycles of doxorubicine – cisplatine were administered.

Fifth cycle was administered on November 2015, with the effect PR, with prolonged hematological and moderate non hematological toxicity. Repeated progression was manifested in six months , and cisplatine – cyclophosphamide was conducted next 5 months with the effect of PR.

This case report presents a nine years long course of disease of the patient with advanced EOC. Patient had a clinically significant partial response to each platinum regimen, which is why this case is an example of a very chemiosensitive cancer. Unfortunately, through the course of time, duration of good response was reduced from initial 24 months to 6 months in the last approach.

Our patient`s case represents a rare example of chemiosensitive disease which has significantly exceeded overall average survival, characteristic to epithelial ovarian cancer, and, at the same time, the course of treatment illustrates the importance of individually tailored therapy.

P13 - Response to treatment with topotecan in patient with recurrent ovarian cancer considering sensitivity to the platinum

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Ovarian cancer is a chemosensitive disease and most of the patients with ovarian cancer have a good response to the first line therapy. Despite of this, 80% of patients will develop recurrence of the disease, most often within the first two years. Topotecan is one of the options of treatment in relapse. In Croatia, topotecan is available in the second and third line therapy of patient with ovarian cancer.

In retrospective study we included 80 patients with ovarian cancer treated with topotecan in our institution in the period from 01.05.2011. to 31.12.2014. The response to treatment with topotecan we analyzed according to RECIST criteria. The patients were divided in 2 groups: 1. who received topotecan as a second line (39 patients) 2. who recieved topotecan as a third line (41 patients). The each group was divided considering to the platinum sensitivity to: 1. refractory 2. resistant 3. sensitive disease.

In the first group responded 5 of 7 patients (71%) with platinum refractory disease, 7 of 24 patients (29%) with platinum-resistant disease, and 4 of 8 patients (50%) with platinum sensitive disease. In the second group responded 6 of 15 patients (40%) with platinum refractory disease, 2 of 15 patients (13%) with platinum-resistant disease and 9 of 11 patients (82%) with platinum sensitive disease.

Topotecan had similar efficacy in the second and in the third line therapy of recurrent ovarian cancer, but more complete responses and a longer time to progression has been observed in patients who received topotecan as the third line. The best response to treatment has been observed in patients with platinum sensitive disease.

P14 - Epidemiologic analysis of patients with testicular cancer during a 5-year period in the Referral center for treatment of germ cell tumors and extragonadal germ cell tumors in Republic of Croatia

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Testicular cancer accounts for approximately 1% of all malignancies in men, but is the most common cancer of younger male population, with the highest incidence between ages 15 and 35. Given that testicular cancer cannot be prevented, it is necessary to diagnose the disease in early stages, because of higher cure rates. If the disease is found early, curability is about 95%, and in advanced stages of the disease curability falls to 60%. Given the published data on the above average increase in the incidence of testicular cancer in Croatia for 7% from the year 1983 to 2007, and projected increase in the incidence of testicular cancer by 72% by the year 2025, we analyzed data of testicular cancer patients in the Department of Oncology, University Hospital Center Zagreb. The aim of the research was to obtain a clear picture of the incidence of advanced stage of testicular cancer patients over five years categorized by Croatian counties, so we could redirect educational programs aimed at raising awareness of the testicular cancer in the most vulnerable areas. In a retrospective study conducted at the Department of Oncology, we analyzed data on patients treated from January 2012 to December 2016. Data were collected using hospital system BIS, and were analyzed by patient age, stage of disease and the county of origin. During the five-year period, the total number of newly diagnosed patients with testicular cancer was 461, mostly between the ages of 30-35 years. The largest number of patients were from Zagreb, including Zagreb County, followed by Brod-Posavina and Koprivnica-Križevci County. Considering the data from Croatian National Institute of Public Health incidence of testicular cancer, about 50% of all newly diagnosed patients with testicular cancer in Republic of Croatia were examined and treated in the Department of Oncology, University Hospital Center Zagreb. During the five-year period, we identified a trend of reduction in newly diagnosed patients with advanced-stage testicular cancer by 20% to 8%. The majority of patients with advanced stage at diagnosis originated from Zagreb and Zagreb County, followed by Međimurje and Karlovac County. Given the impossibility of preventing testicular cancer, substantially higher cure rates can be achieved by early detection. This is further enhanced by public relation media for the purpose of informing and educating targeted male population. Such propaganda was conducted with a campaign for early detection of testicular cancer, *Počeši s razlogom*, which began in March 2016 and won this year's Grand Prix and a gold award Croatia Effie.

P15 - Lung cancer – experience of a small center

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Objective of this study was to determine median overall survival of the patients treated of lung cancer at the Department of hematology and oncology General hospital *Dr. Josip Benčević* in Slavonski Brod, also we analized characteristics of patients and treatment based on medical records. Retrospectively we analized data of 195 patients treated in period of 40 months from 09/2013 to 12/2016. It was 151 men (77.4%) and 44 women (22.6%), median age at the time of diagnosis was 65 years range form 43 to 81 years. There were 84% patients with non small lung cancer (NSCLC), 42% had squamous lung cancer, 31% adenocarcinoma, 9% adenosquamous or large cell carcinoma, 2% large cell neuroendocrine carcinoma, 16% patient had smal cell lung cancer. Of all NSCLC 5% had EGFR mutation, and only 4% of patient had ALK determined. Concerning staging 1.2% classified as stage I, 3.5% as stage II, 22.5% as stage III and unfortunately majority of them 72.8% patients as stage IV. Most of them were smokers (74%) and routinely drinking alcohol (27%). At the time of dijagnosis 60% of patients met criteria for cahexia diagnosis. After the first examination of medical oncologist 15 patients (7.7%) were send to thoracic surgery, and 7 patients (3.5%) were operated after neoadjuvant chemotherapy or neoadjuvant chemoradiotherapy. Chemotherapy was administered primarily in outpatients environments. We analized numbers od chemotherapy lines during treatment of each patient: 46% of patients received only one line of treatment, 27% received two lines, 18% three lines, four and more lines of chemotherapy was given to 9% of patients. Time to progression in first line of treatment was 6.6 months. With concomitant chemoradiotherapy we treated 10% of patients, palliative radiation 18% of patients and intrapericardial chemotherapy for pericardial tamponade in 4 patients (2%). Neutropenia durig first line of treatment was identified in 10% of patients, due to complications of treatment 50% of patients was admitted to our hospital department one or two times, but 22.% patients were never hospitalized. One year survival was 38.6%. Median overal survival was 11.79 months. Due to new studies in lung cancer that are chaging perspectives for some patients recently treated with chemotherapy and prolong survival we hope that for our patients molecular diagnostic methods will be more available in order to select potential candidates for already approved but also for novel treatments in era of individualized oncology treatment.

P16 - What is the future of hormone receptor positive HER2 negative metastatic breast cancer treatment?

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It is estimated that approximately one out of every eight Croatian women will develop invasive breast cancer over the course of their lifetime. Breast cancer is a heterogeneous disease comprising different clinical, histopathological, and molecular subtypes. Estrogen receptor (ER) is expressed in approximately 70% of newly diagnosed breast cancers and has an important role in tumor growth and progression. Endocrine therapy forms the backbone of treatment for hormone-dependent breast cancer. Despite the benefits of endocrine therapy, resistance occurs in a large number of patients and represents an important clinical challenge in the management of breast cancer.

Mechanisms of endocrine resistance and future therapeutical strategies:

Endocrine resistance occurs as intrinsic (*de novo*) or acquired, depending on duration of initial response to endocrine therapies. The most important future approach for treating HR+ breast cancer is one that involves overcoming endocrine resistance. Understanding already identified mechanisms of resistance to endocrine therapies helps us in development of novel potential drugs to overcome resistance. The most important mechanisms of endocrine resistance are: 1. changes in the ER signalling pathway and its coregulators 2. Increased activity or overexpression of tyrosine kinase receptors (RTKs) 3. Increased activity of proteins regulating cell defense mechanisms (Akt, PI3K, mTOR) 4. Changes of cell cycle regulatory proteins (Myc, Cyclin D1). Most of them are results of genomic and epigenomic changes in tumor cells, rarely are reflections of tumor microenvironment and host influences.

The combination of mTOR inhibitors with endocrine agents has been incorporated into clinical practice after the publication of the BOLERO 2 trial, a randomized phase III study which demonstrated significant improvement in PFS with the addition of the mTOR inhibitor everolimus to the steroidal AI exemestane.

A new strategy in treating patients with ER-positive breast cancer is to target cyclin-dependent kinases 4 and 6 (CDK4/6), a key pathway involved in regulation of the G1/S transition of the cell cycle. At the present time, there is no evidence demonstrating a role of specific biomarkers other than ER, PR, and HER2 in the clinical management of HR+ advanced breast cancer. Use of other biomarkers is considered experimental and currently should be limited to clinical trials only.

Metastatic breast cancer still remains an incurable disease for most patients. Advances in understanding tumor biology, particularly signaling pathways, have led to the development and approval of many novel agents. Here we present the well-known mechanisms that lead to the development of resistance to the endocrine treatment as well as the current and future treatment options based on the mechanisms involved.

P17 - Imatinib as second-line treatment for inoperable progressive mesenterial desmoid tumor and familial adenomatous polyposis – a case report

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42-years old female patient was hospitalised at the abdominal surgery clinic, where a progressive abdominal tumour was under work-up and found to be inoperable. A total colectomy for familial adenomatous polyposis (FAP) was performed in the year 2008. The diagnosis of inoperable desmoid mesenterial tumour/aggressive fibormatosis was established 7 years after *via* laparoscopic biopsy. Patient was then treated with tamoxifen 10mg bid during 1 year and with discontinuation, and control CT of the abdomen showed progressive disease. Patient suffered from diarrhea, abdominal tenderness, cystostomy maceration, frequent urinary infections, weight loss and anemia.

Tamoxifen in dose of 40mg bid together with celecoxib 200mg daily was reinduced in treatment as escalation in dose of the first-line treatment. After 4 months the tumor progressed in size and symptoms with newly spontaneous formation of ileo-tumor-cutaneous fistula. Second line treatment with imatinib mesylate was offered in a dose of 400mg daily. After 6 months of imatinib, control CT scan of the abdomen showed no progression and stable disease. Patient still had similary symptoms but reduced in frequency and intensity. Side-effects of imatinib included grade 1 ones: sporadic abdominal pain, fatigue and periorbital swelling. Strategy for further treatment is continuation of imatinib in the same dose until the disease progression.

Imatinib in daily dose of 400mg as a second-line treatment for an inoperable progressive abdominal desmoid tumor was well tolerated and effective in this patient. No progression after 6 months and no grade 2 or higher side effects were observed.

For patients with FAP, total colectomy and subsequent inoperable desmoid tumors, there is a great need for effective novel therapies and their availability, as well as for possibility for recruitment in clinical trials, since this rare disease lacks the standard therapeutical procedures.

P18 - Single institution experience in fertility preservaion in female patients diagnosed with early stage cancer

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This is the review of our experience in fertility preservation in female patients diagnosed with early stage cancer. The aim of the review was to show, whether cryopreservation prolonges time until chemotherapy.

A retrospecitve study was conducted from March 2015 to March 2017 at the Department of Medical Oncology University Hospital for Tumors, Sestre milosrdnice University Hospital Center. Data were collected from medical history.

Out of all female patients which were diagnosed with early stage cancer 40 of them wanted to preserve their fertility. Out of total number 38 patents were diagnosed with early stage breast cancer, and two patients were diagosed with colorectal cancer.

Patients were between 25 and 43 (median 34) years of age, and they were treated in adjuvant or neoadjuvant setting.

All patients were offered with cryopreservation of oocytes or embryos with subcutaneous application of LHRH agonist, or just LHRH agonist application before the start of chemotherapy application or endocrine therapy.

Out of 40 patients nine underwent cryopreservation process. Others opted for monthly subcutaneous LHRH agonist application which was conducted during the whole time of chemotherapy application/ endocrine therapy and continued up to three month after last chemotherapy application.

Medical record analysis showed that average time from patients presentation at Multdisciplinary team to the first application of chemotherapy was 40.2 days in group that underwent oocyte/embryo cryopreservation, and average time for LHRH group was 21.6 days.

Final data of this review is consistent with data available in current literature.

P19 - Our experience with palbociclib

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Clinical efficacy of endocrine therapy (ET) is limited with the development of primary (*de novo*) and secondary resistence to ET. Cyclins and cyclin-dependent kinases (CDK) play a key role in cell signaling and their dysregulation is one of the mechanisms responsible for the development of endocrine resistance. Several clinical studies phase II and III (PALOMA1/TRIO18, PALOMA2 and 3) showed a significant benefit of the combination of CDK inhibitors (palbocicib, ribociklib, abemaciklib) plus ET.

Thanks to Compassionate Use Program, in our institution treatment with palbociclib began on March 3, 2016. Since then, the program included 13 patients, seven have been so far treated (three patients in the course of active treatment) and five patients had not yet begun treatment. The inclusion criteria are: hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer previously treated with a minimum of four therapy lines for metastatic disease. Before being included in the program our patients have previously received an average of five lines of treatment for metastatic disease (4-6). Palbociclib is taken orally once daily on a 28-day cycle consisting of 21 days on the drug and seven days off; letrozole is taken orally once daily. *Median age* (range) is *61 years* (*49-72*). Neutropenia is the most common adverse event.

Dose interruption, dose reduction or delay in starting treatment cycles is not recommended for patients who develop grade I or II neutropenia. Three patients had neutropenia grade III, one febrile neutropenia and they were required to temporary discontinue treatment (3-23 days). The most common *non-hematologic* adverse events were grade I or II: fatigue (4), nausea (3) and diarrhea (2). The median duration of treatment is 15.35 weeks (3-43.5).

Based on our experience we can conclude that palbociclib, in combination with ET, is potentially an *effective therapeutic option*, with a consistent safety profile, in the later lines of treatment luminal, HER2-negative breast cancer.

P20 - Unusual pathohistological finding in patient with prostate cancer

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Our patinet, was a 74- years- old male with no comorbidities or concomitant medications and no family history of malignancy. In january 2008 due to PSA elevation, TURP (transurethral ressection of prostate) was performed and pathohistology report has shown: Adenocarcinoma, G2, Gleason scor 7 (3+4).

Initial PSA was 26.54 ng/ml (point) and bone scan has shown osteoblastic-ostelytic solitary metastasis in thoracic vertebre. After 12 cycles with LHRH agonist, we have registered biochemical response with decreased PSA level of 0.79 ng/ml. In august 2009 when PSA elevation was detected, retreatment with 8 cycles of LHRH agonists was performed. In april 2010 we detected a left pleural effusion /X ray/, generalized lymphadenopathy with hydronephrosis grade 2 and urinaryretention / CT scan/, and biochemistry report has shown azotemia with abnormal liver function test. PSA was 3ng/ml.

Because of this unusual presentation, progression of disease with low PSA, lymph node biopsy was done. Pathohistology and imunohistochemistry report has shown: metastasis of carcinosarcoma wich was negative for PSA and PSAP and CD8 and CD20 positive.

In summary, we conclude that metastatic, carcinosarcoma prostate, and PSA -, and PSAP-negative prostate carcinoma, is a rare and highly aggressive neoplasm with an associates poor outcome.

P21 - Clinical outcome in patients with primary advanced or metastatic endometrial carcinoma treated with standard chemotherapy regimen according different histopathologic characteristics

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Most cancers of the endometrium are of endometrioid histology (type 1 EC). A smaller subset is associated with aging and unique genetic/molecular changes, producing a more aggressive variant, serous/ clear cell type/ undifferentiated (Type 2 cancers). The aim of this study was to investigate difference in clinical outcome in patients with primary advanced or metastatic endometrial cancer treated with standard chemotherapy combination consisting of doxorubicin-cisplatin (DOX-CDDP) with regard to histological subtype.

Eligible patients had histologically-proven advanced and/or metastatic endometrial adenocarcinoma and were chemotherapy-naive. Treatment consisted of CDDP 50 mg/m^2 combined with DOX 60 mg/m^2, every 3 weeks. Response rates were evaluated according to RECIST 1.1 criteria. Kaplan Maier method and Log rank test were used to assess survival prognostic factors. Median age was 64 years (range 34-77). Patients were divided into 2 groups according to histopathology type: Type 1 EC- endometrioid and Type 2 EC- serous/clear cell/ undifferentiated type. Between 2007 and 2012., we analysed 18 patients (60%) with Type 2 EC (6 papillary serous, 11 clear cell, 1 undifferentiated) and 12 patients (40%) with Type 1 EC.

Thirty patients underwent hysterectomy and BSO, with or without lymphadenectomy. FIGO stages were as follows: FIGO III=18 (60%), FIGO IV=12 (40%). Twelve patients (100%) with Type 1 EC had partial and complete remission (responders). Response for Type 2 was as follows: 7 patients (39%) had stable disease (SD) and 11 patients (61%) had partial and complete remission (responders). The combination DOX–CDDP provided a significantly greater therapy response in Type 1 EC compared to Type 2 EC (*Fischer Exact test; p =0.024).* At the time of analysis, 76% of patients were still alive after median follow up of 21 months (9-58). Median progression free survival (PFS) for Type 1 EC was 18 months (range 8-56), and median PFS for Type 2 EC was 11 months (5-26), demonstrating significant TTP difference between Type 1 and Type 2 EC (Log-Rank test; p=0.0014). There was no need for treatment adjustment due to toxicity. Neutropenic fever occurred in 1 patient (3%). The most common nonhematological toxicities were fatigue grade 1-2 (70%) and nausea grade 2 (42%) while 4% of patients suffered from peripheral sensory neuropathy grade 1.

Type 2 endometrial cancer is rare and differs from Type 1, especially with respect to high frequency of distant metastaes. Our results indicate worse outcomes to standard chemotherapy in Type 2 EC compared to Type 1 EC, suggesting multicentric studies are needed to better define appropriate management of those malignancies.

P22 - Tolerability of bevacizumab in triple-negative (TNBC) metastatic breast cancer patients: a single institution experience

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Subset analyses suggest TNBC benefits from angiogenic therapy. Bevacizumab significantly improves progression-free survival and response rate in first-line metastatic breast cancer when combined with paclitaxel. The purpose of this study was to evaluate the safety profile of bevacizumab in combination with paclitaxel in mTNBC patients.

Patients with mTNBC not previously treated with chemotherapy received paclitaxel 80mg/m^2/weekly on days 1, 8 and 15 every 4 weeks with bevacizumab (compassionate use) 10mg/kg every 2 weeks. Patients fullfilled major baseline requirements: no uncontrolled hypertension, no significant proteinuria and ECOG 0 or 1. After achieving maximal therapy response to paclitaxel-bevacizumab combination, bevacizumab monotherapy was administered until disease progression or unexpected toxicity. Patients were prospectively monitored for overall toxicity and for bevacizumab-related adverse events.

Twenty patients were enrolled to treatment between December 2010 and October 2011. The patient population had a rather great metastatic burden: 2 patients had four metastatic sites, 4 had three, 9 had two (2 pts with CNS and liver metastases) and 5 patients had one metastatic site. Significantly more patients had visceral involvement (liver predominantely) than metastatic disease presented with bone and soft tissue metastases. Registered toxicity was as follows: leucopenia grade 3/4 was observed in 3 pts and neutropenia gr 3 in 2 patients; hemorrhage/bleeding gr 1 (epistaxis and rectal bleeding) occured in 9 pts; proteinuria gr 1 was detected in 4 pts, sensory neuropathy gr 1 in 5 pts and myalgia/arthralgia gr 1 in 5 pts. Hypertension gr 1/2 was verified in 4 patients and only one patient had hypertension gr 3 that was also satisfactory controlled with antihypertensive therapy. After two cycles one patient experienced wound-healing complications in breast region which caused an immediate cessation of bevacizumab therapy. Potentially life-threatening events such as arterial and venous thromboembolism, gastrointestinal perforation, bleeding including pulmonary events or left ventricular dysfunction were not registered.

Our results show that the addition of bevacizumab to paclitaxel chemotherapy is relatively safe and well-tolerated therapy in routine clinical practice, confirming predictable adverse events associated with bevacizumab therapy. Paclitaxel-bevacizumab combination may be considered as an option for the first-line treatment of patients with TNBC metastatic breast cancer.

P23 - Nivolumab induced synchronous occurrence of polymyositis and hypothyroidism in a patient with squamous cell lung cancer

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Immunotherapy in the treatment of malignant diseases is based on stimulating the patient's strength of immune response against tumor and presents great potential in improving the effectiveness of the treatment. Alongside the proven efficacy, immunotherapy in treatment of malignant diseases can cause immune-related adverse events different from commonly known chemotherapy-related toxicities.

A 63 years old female patient was diagnosed with stage IV squamous cell lung cancer in February 2015. The first-line treatment was gemcitabine and cisplatin chemotherapy (4 cycles), and soon after disease progression second-line treatment, docetaxel, was applied (4 cycles). In March 2016, after disease progression, patient had started with nivolumab immunotherapy. In the 7th month of nivolumab treatment, the patient complained of a symmetric weakness and a pain in proximal muscles of the lower extremities and in the shoulder girdle musculature. Creatine kinase (CK) and myoglobin levels were significantly elevated: CK level was 2657 U/L while myoglobin level was 226 μg/L. The analysis of thyroid hormones revealed a significant hypothyroidism (TSH > 100 000 mIJ/I). Muscle biopsy revealed a damage of muscle fibers with an inflammatory infiltration with lymphocytes. Myophagocytosis was present. It was a synchronous occurrence of immune-related side-effects - polymyositis and hypothyroidism. Immunotherapy was stopped and the treatment with systemic corticosteroid and thyroid hormone substitution was introduced. The patient reported an improvement in the strength of the affected musculature regions with the disappearance of muscle pain. In follow-up laboratory tests CK level started to decrease. Up to this date, one year after nivolumab treatment started, the patient is without disease progression, PS ECOG 0.

Immunotherapy can result in synchronous occurrence of immune-related series of side effects. These side effects are significantly different from the side effects associated with standard chemotherapy, and if they are not recognized and treated in time, they can lead to significant worsening of the patient's condition as well as fatal consequences.

P24 - Survival data on early, invasive breast cancer patients treated with adjuvant chemotherapy: ten years follow-up in University Hospital Center Zagreb

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According to the Croatian National Cancer Registry, the incidence rate of breast cancer in 2014was 119.2/100 000 population while the mortality rate was 44.8/100 000 population, with a total of 2668 new diagnosed cases and1071deaths caused by breast cancer during 2014. Breast cancer is the most common type of cancer among females in Croatia (26%).

This study was conducted to analyze clinicopathological characteristics and treatment results of early breast cancer in subgroup of women with more aggressive subtypes of breast cancers in which systemic adjuvant chemotherapy was indicated. We analyzed and compared 5 and 10 year survival data of this subcohort of patients with results of the whole cohort diagnosed with early breast cancer in the same period.

153 patients were selected from the study cohort of 215 consecutive patients diagnosed with early invasive breast cancer in University Hospital Center Zagreb, in a period between September 2002 and September 2003. All lymph node positive patients received adjuvant chemotherapy and lymph node negative patients received adjuvant chemotherapy only if adverse prognostic factors were present (adverse tumor grade and size, positive lymphovascular invasion, negative hormone receptor status), together with other modalities of adjuvant treatments.

In our study, the group median tumor size was 2.2 cm, dominant tumor grades were 2 and 3, and 40% of patients had positive axillary lymph nodes. Lymphovascular invasion was present in 7.2% of all tumors. Molecular surrogate subtypes of breast cancer were as follow: luminal A 47.5%, luminal B1 10.4%, luminal B2 8.5%, HER2 overexpressed 9.1% and triple negative 24.8%. All our patients have received adjuvant chemotherapy without adjuvant trastuzumab for HER-2 subtype: anthracyclines 60.7%, CMF 19.6%, taxanes 9.8% and FAC/CMF 9.8%.

During the ten-year follow-up 58 of 153 patients (37.91%) relapsed, and 47 of them (81.03%) relapsed in the first five years. The disease free survival (DFS) in five and ten years follow-ups in our subgroup were 69.28% and 62.09%,whilethe whole group had DFS of 73.97% and 69.90%. The overall survival (OS) in five and ten years follow-ups in our group of 153 patients was 83.66% and 71.89%,and in the whole group of 215 patients was 88.50% and 73.30%, respectively. Out of 215 patients with breast cancer, during the ten-year follow-up, 62 of them (28.83%) relapsed and 55 of them had died (25.58%).

We can conclude that our subgroup has had worse results of DFS and OS during the five and ten years follow-ups in comparison to the group of all 215 breast cancer patients.

Breast cancer patients who received adjuvant chemotherapy have had a more aggressive disease and after adjuvant chemotherapy treatment the most relapses and deaths happened in the first five years of the follow-up. In addition, despite adjuvant chemotherapy and other adjuvant treatment modalities, our group of breast cancer patients had worse results of DFS and OS during the five and ten years follow-ups compared with the group of all 215 patients with early invasive breast cancer.

P25 - Trichiasis as a result of docetaxel chemotherapy for metastatic prosate cancer

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Docetaxel is a chemotherapeutic agent from tihe class of taxanes which works by disrupting microtubule function to inhibit cell division. Docetaxel has been proven as a potent agent in treatment of various solid malignancies, including metastatic prostate cancer. Most adverse events associated with the use of docetaxel have been well documented and are expected, alopecia beeing at the top of the list. Patients are informed to expect not only hair loss, but also loss of ovearll body hair, including eyebrows and eyelashes.

Trichiasis is an eyelid abnormality in which the eyelashes are misdirected and grow inwards toward the eye. Those inward-turning lashes rub against the cornea the inner surface of the eyelids which leads to eye irritation, swelling and redness and in severe cases to scarring of the cornea and vision impairment.

A 62-year old male with no previous comorbidities was diagnosed with prostate cancer after a routine screeing discovered elevated PSA 14,6. After biopsy and imaging the patient was classified as intermediate risk based upon his Gleason score 7 (4+3), and PSA level and underwent radical prostatectomy. PHD was adenocarcinoma, GS7, meta lymphonodi, pT3bpN1M0. After surgery the patient received adjuvant radiotherapy in combination with ADT that lasted for 3 years. In 4/2011 the patient underwent orchidectomy on the count of biochemical relaps of the disease. He continued with ADT, Kalufar 5 mg. The patient was stabile untill 7/2014 when the PSA levels begin to rise, although he had no symptoms and was in overall good health. In 10/2014 PSA was 32,6 and imaging methods (CT and PET scan) showed multiple metatstic lymph nodes and multidisciplinary team suggested chomotherapy with docetaxel which he started in11/2014 and completed in 7/2015. After 2 cycles of chemotherapy the patient lost most of his hair, including eyelashes wich didn't grow back during the 10 cycles of docetaxel he received. 6-8 weeks after completing chemotherapy the patient started complaining of eye iritation, extensive lacrimation and blurred vison, especially on the left eye. He went for an ophtalmological exam and the diagnosis was trichiasis l. sin et dex susp. The ophtalmologist recommended the patient do eyelash epilation and ordered a checkup 4 weeks later to confirm the diagnosis. After the confirmation, the patient continued with mechanical eyelash epilation every 2-3 months. On the last checkup in 12/2016 the ophtalmologist suggested electroepilation as a permanent solution.

Although docetaxel has been reported to cause itching, puffiness, or swelling of the eyelids and loss of eyelashes is very common among patients recieveng this chemotherapy, this specific side effect has not been seen among our patients. It is important to keep in mind that chometherapeutics can cause significant impairment in quality of life long after their last dose has been applied.

P26 - Neutrophil/lymphocyte ratio as a predictive value for treatment outcome after neoadjuvant therapy in locally advanced breast cancer patients

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Inflammation has an important role in cancer progression, as neutrophils and lymphocytes are thought to be significant in tumour immunology and inflammation. Neutrophil/lymphocyte ratio (NLR) is used as a marker of subclinical inflammation. In several malignancies prognostic value of NLR was demonstrated, indicating that elevated NLR determines worse prognosis of the patients.

The aim of this study was to determine the relationship between pretreatment NLR values and pathologic complete response after neoadjuvant therapy in locally advanced breast cancer patients.

Retrospectively we identified 117 patients with breast carcinoma (BC) treated with neoadjuvant chemotherapy (NCT) at University Hospital for tumors in Zagreb. 79 patients finished NCT and underwent surgery so theirs data were further analyzed. Pathological complete response (pCR) was defined by absence of invasive cancer in resected breast and axillary tissue. Value of NLR was measured at the start of neoadjuvant treatment by dividing the number of neutrophils by the number of lymphocytes. Median age was 55 years. Pathological complete response (pCR) was achieved in 24% BC patients treated with NCT (47% luminal B, 53% hormone receptor negative BC). NLR ranged from 0.94 to 5.22. The median NLR values were similar in both pCR and non-pCR arm (2.3 vs. 2.38). Pathological complete response (pCR) was achieved in 31% patients with low NLR (<2.0) and in 19% of patients with higher NLR (>2.0). There were also no significant differences regarding BC subtypes. There was no relationship between the pCR and pretreatment NLR values.

P27 - The treatment of locally advanced or metastatic soft tissue sarcomas in the era of innovative therapies and hystorical review of therapies in Croatia Single center experience – University Hospital Centre Zagreb

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The treatment of locally advanced or metastatic soft tissue sarcomas is still challenging even now in the era of novel, innovative therapies. Historically, the sequencing of therapies for soft tissue sarcomas (before trabectedin, Yondelis® and pazopanib,Votrient®) was not strictly defined. The chemotherapy backbone in the first line of treatment in past decades (but also nowadays) were anthracyclines as monotherapy or in combination with ifosfamide, dacarbazine etc. Second or third line of treatments were combinations of chemotherapy not included in the first line, like gemcitabine or taxanes. With novel therapies like trabectedin or pazopanib we observed not just improvements in PFS (*progression free survival*) or even in OS (*overall survival*) but definitely in quality of life.

We will present our experience with novel therapies and historical review of soft tissue sarcoma treatments in Croatia. We analyzed two cohorts of patients. The first one is historical (around 20pts.), and the second one is the cohort of patients treated with trabectedin and pazopanib in second or third line of treatment (around 50 pts). The results of our analysis will be presented as type of medications used in first, second or third line of treatment and with time to progression intervals (PFS).

P28 - Cancer cachexia, sarcopenia and biochemical markers in patients with advanced non-small cell lung cancer - chemotherapy toxicity and prognostic value

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Cancer cachexia and sarcopenia are frequently observed in cancer patients and associated with poor survival. The majority of studies of cancer cachexia and sarcopenia have been done in patients with solid tumors of different origin, and there are currently no good predictors of the benefit of chemotherapy or factors that predict survival in advanced cancer.

The purpose of our prospective study was to evaluate prevalence of cachexia and sarcopenia using international consensus definition and criteria for diagnosis in patients with diagnosed advanced non-small cell lung cancer (NSCLC) stage IIIB and IV and their relation to chemotherapy toxicity and survival prediction. A secondary aim was to compare several biochemical markers (CRP, IL-6, protein and albumin) with time to tumor progression in order to assess prognostic value or to guide a treatment.

Between December 2013 and April 2015, the prospective cohort study of one hundred Caucasian patients with advanced NSCLC stage IIIB or IV, who were referred consecutively to Department for Respiratory Diseases 'Jordanovac' was evaluated. Anthropometric measurements and biochemical data (CRP, albumin, protein, IL-6, haemoglobin) together with body composition measurements (total muscle cross sectional area, lumbar skeletal muscle index) were obtained for each patient before starting with platinum-doublet therapy. Skeletal muscle cross-sectional area at the third lumbar vertebra was measured by computerized tomography, and sarcopenia was defined using a previously published cut-off point. Toxicity was assessed after cycle 1 of treatment and time-to-tumor progression was determined prospectively.

One hundred patients with advanced lung cancer were recruited: 67 were male, median age was 64 years. The median time to disease progression was 187 days. The prevalence of cachexia and sarcopenia in study cohort was 69%, and 47%, respectively. CRP, IL-6 and albumin concentration in cachectic, compared to non-cachectic patients demonstrated statistically significant difference ($p=0.020$, $p=0.040$, $p=0.003$). Cachexia and sarcopenia were not found to be predictors of chemotoxicity nor time to tumor progression. On the contrary, albumin concentration with established cut-off point of 37.5 g/L was clearly proved as the predictive factor of both chemotoxicity (OR (95% CI) = 0.85; $p<0.001$) and survival (HR (95% CI) = 0.55). Albumin level has shown to be more important predictive marker of chemotherapy toxicity and survival than cachexia and sarcopenia. This approach in clinical settings can be used to guide the choice of oncologic treatment.

P29 - The characteristics and long-term follow up of elderly breast cancer patients treated at Institute of oncology and radiology of Serbia

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Purpose of our study was to analyze the characteristics of elderly patients (pts) treated for breast cancer (BC).

This is a group of 98 elderly (median 70, range 65-79) pts diagnosed with stage I-III BC from Sep/2001 until May/2002. Radical surgery was performed in 80/98 women and postoperative radiotherapy in 66/98 women. The majority of pts had grade 2 (88/98), ductal invasive (49/98), ER and/or PR positive BC (61/98), treated with adjuvant CMF chemotherapy (21/98) and TAM (86/98). The most common co-morbidities were arterial hypertension (67/98) and atrial fibrillation (17/98). After median FU of 109 mos (range 9-148), 24/98 pts experienced BC relapse and 5/98 second primary other than BC. Of 51/98 pts who died, 28/51 died w/o disease relapse. Median disease-free survival was 95 mos (95%CI 74-121); median overall survival was 118 mos (95% CI ^{3} 95).

Age should not be the only limiting factor influencing antineoplastic therapy in elderly BC pts.

P30 - The interactions between herbal preparations and conventional drugs in oncology

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An increasing trend of use of herbal products within the population of cancer patients has been recorded worldwide as well as in our country. A large number of patients without prior consultation with their doctors use the plant products in combination with conventional therapy, which can result in a risk of the emergence of clinically significant interactions. Interactions that may occur between active principles deriving from medical plants and the prescribed cytostatic drugs are based on the same pharmacokinetic and pharmacodynamic principles as well as the interactions which may occur during administration of the actual conventional drugs. Herbal preparations which are used by patients as a supplement to the conventional therapy may directly interact with anti-neoplastic drugs and/or drugs to which patients with cancer use in the treatment of the associated states of comorbidity. The aim of this study was to analyse the potential possibility of arising of interactions with the administration of conventional cytostatic drugs and herbal preparations that are most commonly used. Among the most used herbal preparations there are those that contain active principles derived from medicinal plants such as: St. John's wort (*Hypericum perforatum* L.), Echinacea (*Echinacea sp.),* Ginseng (*Panax ginseng* C.A. Mey), garlic (*Allium sativum* L.), green tea (*Camellia sinensis* L. Kuntze) and peppermint (*Mentha x piperita*). By systematic review of the literature, an overview was made concerning the latest scientific knowledge available in electronic databases such as MEDLINE (PubMed), EMBASE, AMED, CINHAL, Natural Medicines, Google Scholar and Cochrane library database. The review of the current literature has confirmed the pharmacokinetic and/or pharmacodynamic mechanisms of interactions that may occur during the simultaneous use of the most widely used plants and conventional antineoplastic agents where most of the interaction occurred as the result of the mediated metabolic induction or inhibition. St. John's wort is a very used herbal product that acts as a powerful inducer of the CYP3A4 enzyme and P-glycoprotein and its simultaneous administration with conventional antineoplastic agents (irinotecan, imatinib), is a result of a reduction in the bioavailability and therefore the efficiency of the applied drug in therapy. Echinacea is also very often used as an immunestimulant and acts as an inhibitor of the CYP3A4 enzyme so that its simultaneous use with conventional cytostatic drugs is under an increased risk of occurrence of toxicity. Studies show that Echinacea in combination with etoposide can lead to the occurrence of significant thrombocytopenia. The active principles originating from garlic that are applied in combination with an alkylating agent such as cyclophosphamide, result in a reduction of genotoxicity, which leads to the conclusion that the garlic performs induction of CYP2B6 enzyme and reduces the effect of cyclophosphamide. The green tea flavonoids have an antagonistic effect if applied together with an antineoplastic agent bortezomib, so that their simultaneous administration is followed by the absence of a therapeutic effect. Tannins that are present in green tea and peppermint may create chelate complexes if used with the iron preparations which affect their bioavailability. Patients diagnosed with cancer are more inclined to venous thromboembolism. Therefore the administration of warfarin with the St. John's wort and Ginseng is associated with a reduction in efficacy of the drug due to the direct induction of enzymes that metabolise the S and R stereoisomers of warfarin. After examining the available data, we concluded that the use of herbal preparations with the prescribed cytostatic drugs chemotherapy is being increased. Therefore information and patients' education, and the advancement of knowledge, attitudes and behaviours of health workers regarding the interactions is necessary in order to prevent potential risks of clinically significant interactions.

P31 - Correlates of depressive symptoms in breast cancer patients; a cross-sectional study in Croatia

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Depression is often under-detected in cancer patients, as well as particularly in breast cancer patients. Objective of our study was to check whether breast cancer symptoms are associated with depression. This cross sectional study was done from February to April 2015 at Department of Medical Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb. Targeted population was the general population of patients diagnosed with breast cancer and treated in tertiary healthcare institution. We included the consecutive sample of all eligible patients hospitalized or examined in outpatients' clinic during the study period. Patients Health related quality of life (HRQoL) was measured by EORTC QLQ - C30 questionnaire, version 3.0. Our key outcome was the result of Beck Depression Inventory II (BDI-II). The analysis was performed by robust regression, using NCSS 10 Statistical Software (2015) (NCSS, LLC. Kaysville, Utah, USA). Total of 148 breast cancer patients were included. Median (interquartile range) age was 57 (48-65) years. Patients were hospitalized in 30 (20.3%) and treated in outpatients clinic in 118 (79.7%) cases. The overall model was significant ($P<0.001$) with coefficient of determination after robust weighting, $R^2=0.58$. In other words, 58% of BDI-II variance was predicted by the included variables. After the adjustment for all other variables in multivariate robust regression analysis, significant positive association with depression was found in the cases of tumor stage, number of children, fatigue and appetite loss. Significant negative association was found in the cases of age and diarrhea. We can conclude that level of breast cancer patients depression is associated with fatique, appetite loss and diarrhea independently of different clinical, sociodemographic and vital factors.

P32 - Profile of patients with early HER2 positive breast cancer who developed cardiotoxicity during adjuvant trastuzumab in the University Hospital for Tumors

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Cardiotoxicity during trastuzumab therapy is most often manifested as a decrease in left ventricular ejection fraction (LVEF) ≥ 5% with persistent symptoms or ≥ 10% without symptoms. During adjuvant trastuzumab in University Hospital for Tumors, patients are sent every 3 months to a control echocardiography to medical cardiotoxicity tracking.

We analyzed the profile of patients with early HER2 positive breast cancer who developed cardiotoxicity during adjuvant trastuzumab in our institution. A retrospective review of medical records from the Clinic for cardiotoxicity monitoring in University Hospital for Tumors was conducted from 2009 to 2017 and patients with early HER2 positive breast cancer, who during adjuvant trastuzumab temporarily or permanently discontinued treatment due to the development of cardiotoxicity, were selected. From a total of 796 patients who underwent adjuvant treatment with trastuzumab 42 (5.28%) developed cardiotoxicity, which was reversible in 22 (52.38%), and therapy was only temporarily discontinued, and in 20 (47.62%) irreversible forcing trastuzumab treatment withdrawal. The median occurrence of cardiotoxicity was after seven cycles of trastuzumab, respectively after 5.5 months of trastuzumab treatment.

Patients were compared with regard to:

1) Age, with the hypothesis that advanced age is associated with a higher incidence of cardiotoxicity,
2) Side of adjuvant radiotherapy treatment, with the hypothesis of a higher incidence of cardiotoxicity in patients with left sided breast cancer, and
3) Body mass index (BMI), with the hypothesis that BMI increases the incidence of cardiotoxicity.

Analysis of medical records revealed that among 42 patients who developed cardiotoxicity during trastuzumab treatment, 14 patients (33.33%) were older than 60 years in the time of diagnosis, 21 (50%) had a tumor in the left breast with adjuvant radiotherapy treatment performed on the left side of the chest and 23 of them (54.76%) had a body mass index greater than 24.99, which according to world literature is considered overweight.

The results correspond to data that are listed in the available literature.

P33 - Medical cannabis in symptomatic therapy of oncology patients

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Cannabis sativa L. (Cannabaceae) is one of the first plants cultivated by man and one of the oldest plant sources of fibre, food and remedies. To date, 750 constituents have been identified from cannabis. Out of those 750 over 100 are classified as cannabinoids, a unique group of terpenophenolic secondary metabolites. The principal active constituent is delta-9-tetrahydrocannabinol (THC) which binds to endocannabinoid receptors to exert its pharmacological activity, including its psychoactive effect. The other important molecule of current interest is non-psychotropic cannabidiol (CBD). Research of cannabis medical properties has gained worldwide interest after the discovery of two types of cannabinoid receptors, which are G-protein coupled receptors specifically responding to endocannabinoids, phytocannabinoids and related synthetic cannabimimetic compounds. The medical use of cannabis is still controversial and strongly limited by unavoidable psychotropic effects. However, solid scientific data indicated the potential of therapeutic value of cannabis in controlling some forms of pain, relieving chemotherapy induced nausea and vomiting (CINV) as well as treating cachexia and anorexia with no evidence that giving cannabis to the patients would increase illicit drug use in the general population. Various clinical studies have confirmed the antiemetic effect of cannabinoids in patients with CINV. It has been reported that cancer patients downsized opioid dose after adding cannabis in their pain therapy regimen. Poor chemotherapy response and decreased survival is often connected with cachexia. The majority of clinical studies dealing with cachexia and anorexia are focused on AIDS patients, but there is some clinical evidence that cannabinoids could be beneficial for patients with cancer-associated anorexia/cachexia. In conclusion, cannabis and cannabinoids have an acceptable safety profile with side effects which are generally tolerable and reversible. They also show positive results in various clinical trials considering treatment of nausea, vomiting, pain and anorexia/cachexia. Further clinical trials are essential for clearly defining the role of medical cannabis in symptomatic therapy of oncology patients.

P34 - Safety of generic capecitabine Kapetral as maintenance therapy in metastatic colorectal cancer

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Maintenance therapy is continued use of less potent and toxic drugs when maximum response stabilizes after first-line chemotherapy. It can significantly prolong progression-free survival while maintain an acceptable safety profile and improve QoL. Capecitabine is an oral chemotherapy prodrug that is enzymatically converted to 5-fluorouracil, preferentially in tumor tissue through exploitation of higher intratumoral concentrations of thymidine phosphorylase.

The aim of this study was to evaluate safety of generic capecitabine as maintenance therapy after first-line chemotherapy in metastatic colorectal cancer.

From 10/2016. - 3/2017. we followed and retrospectively analyzed data from 56 patients who were receiving Kapetral as maintenance therapy for metastatic colorectal cancer after 8 cycles of irinotecan-based induction chemotherapy. Initial capecitabine dose was 1250 mg/m2 taken twice daily during 14 days in three week cycle. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (v4.0, 2010). Dose of capecitabine was reduced according to spc recommendations.

More then half patients receiving Kapetral had hand and foot syndrome (52%), 36% had diarrhea, 12,5% hyperbilirubinemia, 14% abdominal cramps, 5% abdominal pain, 9% fatigue, 9% elevated transaminase, 5% hyperlacrimation and 4% of patients had chest tightness. Main dose limiting capecitabine monotherapy adverse events were hand and foot syndrome (34%) and diarrhea (12,5%). Adverse events were more frequent in females and elderly patients (>65y).

The most common dose-limiting capecitabine monotherapy adverse effects are hand-foot syndrome and diarrhea and they can significantly diminish quality of life. It is very important to monitor and report adverse events in our everyday practice.

P35 - Impact of increased body mass index on neoadjuvant treatment outcome in breast cancer patients

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Obesity is a major health issue. It has been associated with increased risk of breast cancer (BC) and poorer prognosis. There is evidence that obese patients are less likely to achieve pathological complete response (pCR) to neoadjuvant chemotherapy (NCT). Although the underlying mechanism is unknown, it is suggested that increased circulating levels of estrogen, insulin, insulin-like growth factor and other hormonal factors in obese patients may promote proliferation of breast cancer cells.

The aim of this study was to determine the impact of increased body mass index (BMI) on pathological complete response in patients with primary BC treated with neoadjuvant chemotherapy.

Retrospectively we identified 117 patients with breast carcinoma treated with NCT at University Hospital for Tumors in Zagreb. 79 patients finished neoadjuvant chemotherapy and underwent surgery so theirs data were further analyzed. Patients were categorized according to BMI: normal weight (<25 kg/m2), overweight (25-30 kg/m2) and obese (>30 kg/m2). Pathological complete response (pCR) was defined by absence of invasive cancer in resected breast and axillary tissue.

Pathological complete response (pCR) was achieved in 24% breast cancer patients treated with NCT (47% luminal B, 53% hormone receptor negative BC). 65% of patients had BMI> 25 kg/m2, from which 29% had BMI >30 kg/m2. pCR was achieved in 14% of patients with BMI >25 kg/m2, in group with s BMI <25 kg/m2 pCR was achieved in 43% of patients. Subgroup analysis showed that patients with BMI> 25 kg/m2 were mostly postmenopausal (90%) and they presented more frequently with luminal B cancer (65%).

Patients with BMI>25 were less likely to achieve a pCR to NCT compared with patients with BMI<25. Obese patients present more frequently with larger, locally advanced breast tumors, so they are more frequently candidates for NKT. Further investigation of mechanism of influence of BMI on treatment outcome is needed. Suboptimal dose of chemotherapy for obese patients may also contribute to diminished efficacy of NCT.

P36 - Opiophobia in cancer patients

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Strong opioids like morphine are the mainstay of cancer pain treatment. Some patients are reluctant to use morphine due to fears and misconceptions. Opiophobia is the reason for undertreatment of chronic cancer pain despite the availability and access to these medications.

Objective of our study was to dentify concerns,fears and misconceptions about opioid analgesics among cancer patients who previousy hadn't been treated with these medications.

Spontaneous patients statements concerning fears of opoids were collected when opiod was prescribed for the first time.

Only 12 out of 120 patients had no concerns using opioid analgesics. The majority of our patients (108/120) were reluctant to use opioids. In total, 18 different statements that indicate presence of opiophobia, were collected. The five most frequent categories were identified: concerns about tolerance, addiction and adverse events, fear that the treatment implies the end of life and fear that the patient might be considered weak and unable to endure pain.

Most of the patients were unwilling to use prescribed morphine for the treatment of cancer pain. The five most frequent categories of statements explaining the reasons for the reluctance to use morphine were identified and will be used for patient education and counselling in order to improve cancer pain treatment.