

A Case of Small Cell Lung Cancer with De Novo Psoriasis During Immunotherapy

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Introduction: The immune checkpoint inhibitors, which have been used successfully in many cancers, have started to be used first as a third-line treatment agent, and recently as a first-line treatment agent in the treatment of small cell lung cancer (SCLC). The efficacy of this treatment is associated with many immune-related adverse events, including skin toxicity. Although skin toxicity with immunotherapy is usually in the form of rash and pruritus, rare reactions such as psoriasis can also be seen. Herein, we present the development of psoriasis and complication management in a patient receiving immunotherapy for SCLC.

Case: A 51-year-old female patient under first-line treatment with cisplatin and etoposide with the diagnosis of advancedstage SCLC were admitted to our clinic after progression. As third-line treatment, nivolumab was started to the patient with progressive disease after eleven cycles of irinotecan treatment, taking into consideration her good performance status (ECOG: 0). One week after the fourth cycle of nivolumab, erythematous and scaly plaques were seen on the trunk, neck and extremities of the patient (Fig. 1a–c). The general appearance of the lesions was consistent with psoriasis and the diagnosis was confirmed by biopsy. The plaques regressed with topical high-power steroid treatment and immunotherapy was continued under dermatological treatment without any further complications.

Conclusion: In conclusion, rare immune-related adverse events such as de novo psoriasis may develop with immunotherapy. With their expanding role, timely recognition and treatment of these agents are important in the treatment of cancer patients.

Keywords: Immunotherapy, nivolumab, psoriasis, small cell lung cancer

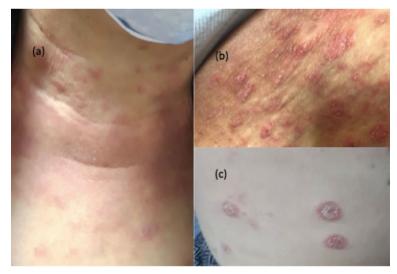


Figure 1. Psoriasiform lesions on the neck (a) and extremities (b-c) of the patient.



Extended Survival with Lapatinib and Capecitabine in a Patient Diagnosed with Trastuzumab-Resistant Metastatic Breast Cancer

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A 55-year-old female patient was admitted to our clinic on August 2011, with the complaint of masses located at bilateral breasts. On physical examination, malignant mass of 1 cm diameter at the 2 o'clock position on the left breast, and a malignant mass of 2 cm diameter at the 2 o'clock position on the right breast were detected. Bilateral breast prophylactic mastectomy and axillary dissection were performed since the results of the breast biopsies revealed that the masses were malignant. Based on the pathology results after the operation, the patient was diagnosed with stage 2 bilateral invasive ductal breast cancer. Breast pathology revealed hormone positive, cerb2 +++ staining. Distant organ metastasis was not detected in radiological examinations. After bilateral prophylactic breast surgery, the patient was prescribed with adjuvant chemotherapy (4AC + 4 docetaxel) and trastuzumab treatment. After chemotherapy is completed, adjuvant trastuzumab treatment was continued upto 1 year. The patient received the final trastuzumab treatment on December 20, 2012. In addition, after the chemotherapy, hormonotherapy (anastrozole) was initiated. In March 2013, upon detection of extensive bone metastases and lung metastases in radiological examinations, the cancer was considered as trastuzumab-resistant and lapatinib + capecitabine treatment was initiated. Lung metastases were verified by biopsy before treatment. In the follow-ups, partial response was observed. In the 5th year of her treatment, the patient had complaints of cough and in the PET/CT performed on 31.10.2017, progression in the mediastinal metastases were observed. Second line trastuzumab-emtansine treatment was initiated. In response, the disease was stabilized. Since the patient had headaches after the 9th cycle, in the brain MR and PET/CT performed on 03.08.2018, brain metastases were detected. The patient received palliative cranial radiotherapy. Palliative care was planned for the patient. After 6 months, the patient died due to progression.

Keywords: Breast cancer, survival, drug resistance



Pancreatic Cancer, Single-Center Experience - Retrospective Analysis

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Introduction: The data of 67 patients diagnosed with pancreatic cancer, followed up and treated by Gulhane Training and Research Hospital, Department of Medical Oncology between January 2012 and August 2019 were retrospectively examined.

Results: Of 67 patients, 63% were male and their mean age was 62.6 years while 37% were female and their mean age was 63.6 years. 56.7% of the patients were stage 4, 17.9% were stage 3, 19.4% were stage 2, 6% were stage 1 at the time of diagnosis. 28.3% of the early-stage patients underwent surgery and adjuvant chemotherapy as the first treatment option. 36.8% of the patients were treated with gemcitabine as a single agent, 15.8% with gemcitabine + capecitabine, 10.5% with cisplatin + gemcitabine, 10.5% with XELOX and other options such as FOLFIRINOX, cisplatin as a single agent, cisplatin + etoposide were preferred for other patients. 47.4% progressed to metastatic stage in their follow-ups. 85% of 67 patients were treated as metastatic stage at the time of diagnoses and/or follow-ups. 28% of these patients received cisplatin + gemcitabine as a first-line treatment option, 26% gemcitabine as a single agent, 15.8% FOLFIRINOX, 8.7% FOLFOX, 5.3% gemcitabine + NAB paclitaxel and other treatment options. 89.5% of these patients died during follow-up. 15.8% of stage 4 patients at the time of diagnosis were still alive and 84.2% died. The maximum survival time is 22 months and the mean survival time is 6.2 months. Survival rate for 6 months was 50% and it was 29% for 12 months. 33.3% of stage 2 patients were still alive and 66.7% died. Survival rate for 6 months was 84.6% and it was 53.8% for 12 months. Four stage 1 patients are still alive.

Conclusion: The treatment responses and survival rates of the patients followed up with the diagnosis of pancreatic cancer were consistent with the literature. More data will be obtained with the addition of new cases. Recently, FOLFIRINOX, gemcitabine + NAB paclitaxel options are more widely used in the treatment of new cases and it is experienced that the contribution of these options to survival is more.

Keywords: Cisplatin, gemcitabine, pancreatic cancer, survival



Is Enzalutamide Safe in Patients with Metastatic Prostate Carcinoma Undergoing Hemodialysis?

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Introduction: In prostate carcinoma, castration resistance (CRPC) develops in all patients after a period of diagnosis. Although docetaxel prednisolone (DP) is the first treatment in which contribution to survival in mCRPC was shown, the survival advantage of hormonal treatments such as abiraterone (AA) and enzalutamide (ENZA) before and after DP has been shown. DP can be used in patients undergoing hemodialysis. The efficacy and reliability of hormonal agents in hemodialysis patients are unknown. While prednisolone is the preferred steroid in PC, it has been shown in a study that dexamethasone provides a survival advantage over prednisolone in mCRPC patients. Herein, we wanted to share the results of enzalutamide in a patient diagnosed with mCRPC undergoing hemodialysis.

Case: A 76-year-old male patient was diagnosed with hypertension and CRF. He has been undergoing hemodialysis (HD) for 7 years. In 2014, he was diagnosed with PC with bone metastasis and goserelin was started. After 3 years, PSA increase was detected. In PSMA PET imaging, extensive metastases were detected in intraabdominal lymph nodes and bones. The patient did not want to receive treatment. In the second month of the follow-up, generalized bone pain, loss of appetite and weight loss occurred. 50 mg/m² DP was started every 2 weeks. Grade 2 thrombocytopenia occurred after one cycle of the treatment. His symptoms regressed. The platelet count was below 100.000/mm³ for one month. After a 1-month treatment-free period, enzalutamide 160 mg/day was started upon the recurrence of his symptoms. After 2 weeks of use, his symptoms completely regressed. PSA decreased. Hemorrhagic stroke occurred in the 4th month of the treatment. Stroke was evaluated depending on insufficient dialysis and insufficient blood pressure control. PSA progression occurred concurrently. The treatment was continued because he was clinically and radiologically stable. When symptomatic and radiological progression occurred in the 9th month of the treatment, dexamethasone 1 mg/day was added to the treatment. One month after dexamethasone, symptomatic complete response was obtained. PSA increase rate decreased. When he experienced clinical and radiological progression in the 16th month of the treatment, the treatment was discontinued and bone-targeted palliative radiotherapy (RT) was given. The patient whose performance regressed to ECOG 3 at the end of RT died at the 17th month of the treatment.

Conclusion: We wanted to emphasize two points with this case. First, enzalutamide can be used safely in HD patients. Second, the use of dexamethasone with enzalutamide is not mandatory, but it may provide a survival benefit.

Keywords: Dexamethasone, docetaxel, enzalutamide, hemodialysis, prostate carcinoma

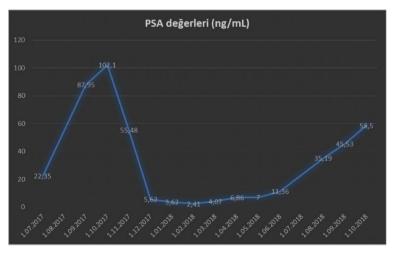


Figure 1. PSA values.



A Rare Case of Solid Papillary Breast Carcinoma

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Introduction: Solid papillary breast carcinomas are low-grade tumors originating from the ductal epithelium of the breast. They are commonly known as in situ tumors and often show neuroendocrine differentiation. Median age at incidence is 72 and it is a very rare type in postmenopausal period. It occurs less than about 1% in all breast cancers. Herein, we aimed to present a case of solid papillary breast carcinoma detected incidentally at control visit, without any complaint of the patient.

Case: A 77-year-old postmenopausal female patient had a 13x7 mm lesion in her left breast 2 cm away from the areola at 11-12 o'clock position in her breast ultrasonography performed during routine controls. Tru-cut biopsy revealed solid papillary carcinoma with positive hormone receptors and neuroendocrine differentiation. The biopsy showed suspicious foci in terms of invasion. Simple mastectomy was performed to the patient. Microscopy of tumor specimens with two distinct foci in the mastectomy material and measured as 1.5 and 1 cm showed a well-circumscribed neoplasm formed by epithelial clusters whose nuclear grade is 1. Hormone therapy was started to ER 100% PR 95% positive patient in whom suspicious foci in terms of invasion were observed. The patients is still under treatment and follow-up.

Conclusion: Solid papillary breast carcinoma is rare and it is usually diagnosed by routine screening. Although it is considered as in situ carcinoma, some authors have shown that it can progress as invasive carcinoma. Being pathologically low grade, it often shows mucinous and neuroendocrine differentiation. While low-grade neoplasm may be accompanied with conventional invasive breast carcinoma, this neoplasm may exhibit stromal infiltration characteristics as well. When accompanied with conventional invasive carcinoma, patient management should be planned according to the size, grade and receptor characteristics of this tumor. However, in cases of solid papillary carcinomas with stromal infiltration characteristics, it is recommended to plan patient management by staging them like in situ neoplasm. The optimal treatment after histopathological diagnosis is surgery. The prognosis is very good in the absence of invasive carcinoma component. Postoperative endocrine treatment is controversial; thus it should be kept in mind that treatment may vary depending on the presence or absence of invasion.

Keywords: In situ neoplasm, neuroendocrine differentiation, solid papillary breast carcinoma

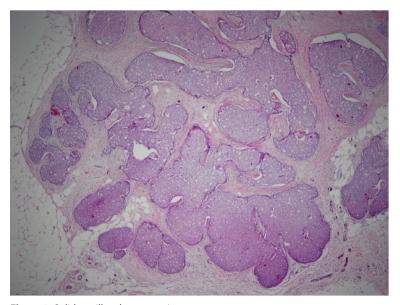


Figure 1. Solid papillary breast carcinoma. Nuclear grade 1 solid papillary carcinoma composed of well-circumscribed solid-cellular nodules separated by fibrous stromal bands.



A Rare Side Effect Due to Cetuximab: Eyelash Elongation

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Case: 12 administrations of adjuvant 5-fluorouracil + oxaliplatin + folinic acid (FOLFOX) chemotherapy was given to the patient operated due to colon adenocarcinoma. The patient, whose adjuvant treatment was completed and who was in follow-up, was diagnosed with prostate adenocarcinoma (GLEASON GRADE 4,5; SCORE: 9, T3b) 2 years later and radical prostatectomy was performed. Immunohistochemical result of cytological examination of the pleural effusion detected in patient follow-up was consistent with colon adenocarcinoma metastasis. 5-fluorouracil + irinotecan + folinic acid (FOLFIRI) treatment was started to the patient due to metastatic colon adenocarcinoma and cetuximab was added in the 4th administration of the treatment, upon the submission of analysis result of K-RAS, N-RAS and BRAF mutations as wild-type. After 5 more administrations of FOL-FIRI + cetuximab, the patient had papulopustular rash on skin and elongation of the eyelashes. Capecitabine + bevacizumab treatment was started because of increased ascites and omental involvement observed in the control thorax-abdomen-pelvic CT of the patient.

Discussion: Cetuximab is a targeted chimeric epidermal growth factor receptor (EGFR) inhibitor molecule used in metastatic colon cancer, especially in patients without RAS mutation. Skin side effects are the most common side effects of cetuximab, and rash and acneiform lesions are frequently seen. Like panitumumab, another anti-EGFR molecule, skin side effects of cetuximab are also evaluated in proportion to the response to cancer treatment in patients. Elongation of the eyelashes due to cetuximab is quite rare, unlike other skin reactions of cetuximab. In the literature, there are studies in the form of case report. In our case, elongation of the eyelashes, a rare side effect due to cetuximab, was observed. The patient did not respond to cetuximab and progression was seen in metastatic colon cancer. In contrast to other skin reactions, the value of cetuximab side effect seen as elongation of the eyelashes in predicting treatment response is seen as low in this case.

Keywords: Colon cancer, cetuximab, eyelash elongation



Gastric Metastasis of Merkel Cell Carcinoma: Case Report

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Introduction: Merkel cell carcinoma (MCC) is the primary neuroendocrine tumor of the skin. Staining with cytokeratin 20 (CK 20) is reported at a rate of 90% in MCC. MCC is a very rare tumor and usually occurs with nodular lesions in the head and neck region in older men. Although it is known to be sensitive to chemotherapy, the response to chemotherapy is poor in metastatic cases. The most common sites of metastasis are skin, liver, lung and regional lymph nodes. Gastric metastasis of MCC is very rare and in the form of case reports in the literature.

Case: A 79-year-old male patient noticed a mass in the gluteal region in May 2009. The mass was excised by the referred physician and its pathology was reported as Merkel cell carcinoma. No distant metastasis was detected in PET CT performed for initial staging. Then, 48 sessions of radiotherapy were applied at the external center for local control. There was no recurrence or residue in the control PET/CT performed in December 2009. The patient admitted to the emergency department in February 2010 because of numbness in the hands and weakness of the lower extremities was hospitalized due to acute neurological syndrome. Brain CT performed to the patient who lost his consciousness during his hospitalization in the neurology service was reported to be consistent with leptomeningeal carcinomatosis. After malignant cell infiltration was detected in the CSF examination, he was transferred to the oncology service with the diagnosis of metastatic Merkel cell carcinoma. The patient received intrathecal 16 mg methotrexate and 8 mg dexamethasone for 2 days. Systemic chemotherapy was not given because of low performance status of the patient. Then, he had melena in the clinical follow-up and upper GIS endoscopy performed by Gastroenterology department revealed a 4 cm bleeding mass in the stomach corpus. Biopsy was taken from the mass and bleeding was controlled by sclerotherapy. Biopsy revealed Merkel cell carcinoma metastasis.

Discussion and Conclusion: MCC is an aggressive skin tumor with high potential for metastasis. Its histopathological diagnosis is difficult. Local recurrence rate is 55-79% and metastasis rate is 50% in MCC. Gastric metastasis is very rare and present with obstruction or bleeding. We decided to present it because it is a very rare tumor and a rare metastasis.

Keywords: Gastric metastasis, merkel cell carcinoma, skin



Effects of Different Radiotherapy Schemes on Survival in Metastatic Malignant Melanoma Patients Receiving Ipilimumab

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Introduction: Despite all the advances in cancer treatment, malignant melanoma is an aggressive type of cancer that progresses very rapidly and has the potential to metastasize in the early period. In recent years, many studies supporting the synergistic effect of radiotherapy (RT) and immunotherapy have been carried out. In this study, the effect of different RT fraction doses and schemes in metastatic malignant melanoma patients receiving ipilimumab was investigated.

Methods: The data of 24 metastatic malignant melanoma patients receiving ipilimumab and RT between 2010 and 2014 were retrospectively examined. Patients were divided into 3 groups according to their RT fraction numbers as ≤ 3 , ≤ 5 and > 5; and they were divided into 2 groups according to the daily fraction dose amount as ≤ 3 Gy and >3 Gy. Among these groups, survival rates were analyzed using Kaplan-Meier analysis. A p value of < 0.05 was considered as significant.

Results: Of the 24 patients included in the study, 13 were female and 11 were male, and there were no surviving patients during the study. The mean survival time of all patients was calculated as 27 months. When separated by the groups, the mean survival time was 25.3 months in 7 patients in the fraction number \leq 3 group, 31.5 months in 6 patients in the \leq 5 group and 23 months in 11 patients in the >5 group (p=0.038). According to daily fraction doses, survival time was 25.6 months in 11 patients in the \leq 3 Gy group and 28.1 months in 13 patients in the >3 Gy group (p=0.073).

Conclusion: Considering the findings of the study, shorter-term and higher fraction doses of radiotherapy seem to be more efficient in metastatic malignant melanoma patients undergoing immunotherapy. This effect may be associated with greater abscopal effect at higher fraction doses, but randomized studies to be conducted with higher patient numbers are needed to clearly assess this.

Keywords: Fractionation, ipilimumab, radiotherapy



Neuroendocrine Tumor of the Breast

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Introduction: Primary neuroendocrine carcinomas of the breast are seen quite rarely. They are indistinguishable because their imaging methods are not pathognomonic findings. The definitive diagnosis is made by pathological examination. We reported a case of neuroendocrine carcinoma, presented with metastatic breast carcinoma in our clinic and underwent surgery due to progression of the breast mass after systemic treatments.

Case: Mammography and breast USG performed due to palpable masses in both breasts in a 46-year-old female patient revealed two BIRADS 5 masses, one with a diameter of 5.5 cm in the right breast and the other with a diameter of 1.5 cm in the left breast. Intracystic papillary carcinoma (ER 100%, PR-, CerbB2-) was detected in the pathology of the patient undergoing left BCS and SLNB in an external center. Tru-cut biopsy of the right breast revealed invasive lobular carcinoma (ER 90%, PR-, CerbB2-). Paclitaxel 80 mg/m²/week was started to the patient in whom bone metastases were detected in bilateral iliac wings, sacrum, left acetabulum, right ischium and left femur in PET/CT and switched to anastrozole after 18 weeks. In May 2016, first exemestane, then fulvestrant was started to the patient whose bone metastases progressed. In March 2017, 6 cycles of EC (epirubicin/cyclophosphamide) chemotherapy protocol was given to the patient with new metastasis in liver. Maintenance treatment with capecitabine was started. First docetaxel+capecitabine followed by ribociclib + letrozole with early access program was started to the patient in whom metabolic and anatomic progression was detected in the right breast mass. After 4 months of treatment, bone lesions were regressed and gemcitabine+vinorelbine treatment protocol was started due to the progression of the mass in the right breast. 42.5 Gy/16 Fr RT was applied to the breast and then mastectomy was performed due to the enlargement of the breast mass under treatment and the responsiveness of systemic metastases. The pathology revealed neuroendocrine carcinoma (ER, PR, CerbB2-, Ki 67: 80%, chromogranin+, synaptophysin+). Chemotherapy protocol was planned for cisplatin etoposide.

Conclusion: In the case of De novo metastatic breast cancer, neuroendocrine carcinoma was detected in the operation performed due to the progression of the primary mass while metastases regressed with systemic treatment. It may be due to the progression of the neuroendocrine component of a previous mixed carcinoma or neuroendocrine transformation of primary cancer. For histopathological diagnosis, biopsy should be taken from isolated progressive areas under treatment.

Keywords: Breast cancer, metastasis, neuroendocrine tumor



The Sign of Leser-Trélat in the Diagnosis of Gastric Adenocarcinoma: Case Report

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Introduction: In the 1800s, Edmund Leser and Ulysse Trelat described spider angiomas seen in oncology patients. Although Hollander associated seborrheic keratosis with malignant diseases in 1900, its name remained the sign of Leser-Trelat. The sign of Leser-Trelat is an increasing number of seborrheic keratoses appearing suddenly especially in the neck, itchy, often accompanied by an internal organ malignancy. It is a rare paraneoplastic incident. It is most commonly seen in gastric adenocarcinoma. It may also accompany pancreas, colon, liver, breast cancers, mycosis fungoides, Sezary syndrome, leukemia and lymphomas. The mechanism of formation is explained by the proliferative effect of tumor-secreted epidermal growth factor (EGF) and transforming growth factor a (TGFa) on keratinocytes.

Case: A 49-year-old male patient without any known disease other than hypertension was admitted to the emergency department with the complaint of hematemesis. In his anamnesis, he stated that he had 16 kilograms of weight loss for the last 8 months, dyspeptic complaints and pruritus. Physical examination of the patient revealed pale conjunctiva, 30x20 mm rigid fixed lymphadenopathy in the left anterior cervical region, and well-circumscribed brown lesions higher than the level of the skin starting from the neck and spreading to the back (Fig. 1). It was thought that these lesions could be the sign of Leser-Trelat in the patient with weight loss and gastrointestinal bleeding. Endoscopy was performed for gastrointestinal malignancy. Endoscopy revealed a 5 cm ulcer malignant in appearance in the antrum and the patient from whom biopsy was taken was hospitalized to the oncology department. During hospitalization, the lesions on the back and neck spread to the arms and the back of the foot. Gastric endoscopic biopsy was reported as adenocarcinoma.

Conclusion: Although the recognition of skin lesions that may be associated with gastrointestinal cancers may contribute to better detection of primary disease and better prognosis in certain situations, it is stated in the literature that some paraneoplastic syndromes may be associated with worse prognosis. Progression was detected in the patient we presented after 3 cycles of DCF treatment. The patient received supportive treatment because of poor performance and died 2 months later. He showed a poor prognosis with a survival time of approximately 6 months from diagnosis.

Keywords: Gastric cancer, leser-trelat, paraneoplastic syndrome



Figure 1. The sign of Leser-Trelat. Nuclear grade 1 solid papillary carcinoma composed of well-circumscribed solid-cellular nodules separated Lesions on the back of the patient.



Long-Term Survival Results with Nivolumab (NIVO) in Patients with Previously Treated Advanced Non-Small Cell Lung Cancer (NSCLC): Effect of Early Disease Control and Response

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CheckMate (CM) 017, 057, 063 and 003 are NIVO studies, which include comprehensive follow-up of previously treated advanced NSCLC patients. Using the data collected from these studies, we evaluated the long-term benefit of NIVO (up to 4 years) and the effect of early response or disease control on subsequent long-term OS. Progression-free survival (PFS) and OS were estimated for patients with NSCLC in all histologies treated with NIVO in combined analyzes of CM 017, 057, 063 and 003 (n=664) and patients randomized to NIVO (n=427) or docetaxel (DOC; n=427) in the combined analysis of CM 017/057.

Other analyzes for CM 017/057 included 6 OS prediction in patients who survived at 6 months according to the response status at 6 months and OS prediction from response time in all responders (complete or partial response [CR / PR]). In the combined analyzes of four studies, 4-year OS rates with NIVO in all patients and in patients with PD-L1 ≥1% and <1% were 14%, 19% and 11%, respectively. In CM 017/057, the 4-year OS rate with NIVO was higher in all patients compared to DOC (14% vs. 5%). At 6 months, subsequent OS with NIVO of patients with CR / PR or stable disease (SD) was longer compared to DOC; 1-year OS rates were higher with NIVO than DOC, while 2-4-year OS rates were similar for patients with progressive disease (PD) at 6 months (Table 1). For responders (CR/PR) in CM 017/0557, the 4-year OS rate from response time was 54% and 12% with NIVO and DOC; the median response time was 24 months and 6 months, respectively. In general, the rate of discontinuation of NIVO treatment due to treatment-related adverse events (AEs) was 8.7%; the most common treatment-related AEs were skin reactions (incidence rate, 38.6 per 100 patient-years). These combined analyzes show significant OS benefit with NIVO in patients with CR/PR or SD at 6 months; this long-term benefit improved further compared to patients who had the same response status with DOC at 6 months. NIVO safety profile was consistent with previous reports.

Keywords: Non-small cell lung cancer, nivolumab, survival

Table 1. 6-month OS turning point analyzes in combined CM 017/057a according to the response status at 6 months a

% of patients living at 6 months	Response status at 6 months %b	1-year OS rate after turning point, %	2-year OS rate after turning point, %	3-year OS rate after turning point, %	4-year OS rate after turning point, %
NIVO 3 mg / kg Q2W (n = 280)	CR / PR, 25	81	63	61	58
	SD, 24	58	35	24	19
	PD, 51	40	13	8	4
DOC 75 mg / m2 Q3W (n = 264)	CR / PR, 13	62	38	26	12
	SD, 39	35	18	7	2
	PD, 48	22	12	8	5

a 6-month turning point time allowed significant time for OS assessment after turning point, while the emergence of the majority of responses with NIVO was used to allow time: time to median response, 2.1 months; 75th quarter, 3.5 months, b % of patients living at 6 months



A Case of Malignant Melanoma with Bi-Cytopenia Induced by Anti-Pd-1 Antibody

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Nivolumab, the anti-programmed cell death 1 antibody, is a promising agent for many cancers. Immune side effects associated with Nivolumab have been frequently defined. However; bi-cytopenia with nivolumab is rare. A 73-year-old man was diagnosed with primary nasopharyngeal malignant melanoma, and liver, lung, and lymph node metastases were detected. Firstly, dacarbazine monotherapy was started to BRAF-negative patient and primary targeted palliative RT was applied. After three cycles of dacarbazine monotherapy, 2 mg/kg nivolumab was administered to the patient with worsened general condition and new metastatic lesions in the lung every 3 weeks. In the 6th administration, anemia and thrombocytopenia occurred in the patient whose general condition improved after the first three administrations, all metastatic lesions in the lung regressed after 7 administrations and metastatic lesions of the liver reaching a maximum diameter of 2 cm were found to shrink. There was a need for intermittent blood transfusion. High dose intravenous methylprednisolone was given to the patient whose Hb decreased to 6.7 g/dL and platelet count decreased to 23000 after seventh administration, but it was ineffective. The patient died 4 months after the onset of nivolumab. In this case, although the mechanisms of Bi-cytopenia are not clear, they may be induced by nivolumab.

Keywords: Anemia, melanoma, nivolumab, thrombocytopenia



Third Line Nivolumab Experience in Metastatic Colon Cancer

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From the examinations of a 30-year-old woman presented with weight loss and abdominal pain, colonoscopy revealed a mass in the rectum, and biopsy from the mass was consistent with adenocarcinoma. In November 2018, the patient underwent emergency surgery due to ileus and left salpingo-oophorectomy and left segmental colectomy were performed while examinations were being carried out. PET/CT examination performed for disease staging revealed a single lesion in the liver, multiple intra-abdominal lymph nodes and peritoneal metastasis. Modified folfox 6 and panitumumab treatment was given for RAS wild-type stage 4 disease. Multiple metastases in the liver, progression in intra-abdominal lymph nodes and omental involvement, and new extensive metastatic lesions in the lung were detected in PET/CT performed for response evaluation after 3 months of treatment. Folfiri-Bevacizumab combination was given as the second-line treatment. Bevacizumab-induced suprapubic enterocutaneous and enterovesical fistula occurred after the 5th administration. The treatment was discontinued and significant increase in the size and metabolic activity of the lesions in the existing metastatic areas and progression were detected in PET/CT performed for response evaluation. Immunohistochemical MSI (microsatellite instability) testing of the primary mass resection material was evaluated as MSH-High with loss of MSH 2 and MSH 6. 3mg/kg Nivolumab treatment was started to the patient every 14 days. Approval of the Ministry of Health was obtained for the treatment. PET/CT performed after 4 administrations showed a 20% reduction in the size of the lesions in the liver, a 75% decrease in their activity, complete response in the lung lesions, a 50% reduction in the mesenteric lesions and a 80% decrease in their activity, a 50% reduction in the size of the intra-abdominal lymph nodes and a 80% decrease in their activity. From the fistulas, enterovesical fistula was closed. Significant regression was achieved in the enterocutaneous fistula. In the patient, who received the 7th administration of the current treatment in August 2019 and continued the treatment, clinically increased appetite and weight gain from 40 kg to 53 kg during immunotherapy were achieved. The need for analgesic treatment decreased by 90%. Immunotherapy is being continued.

Keywords: Colon cancer, immunotherapy, nivolumab



Uterine PEComa: Case Report

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Introduction: In recent years, a group of tumors called "perivascular epithelioid cell tumors" (PEComa) have been reported with increasing frequency from a wide variety of anatomical regions. Although this condition, usually encountered in women, is commonly seen anatomically everywhere, uterus and retroperitoneum appear to be the most common sites of origin of these lesions. PEComas belong to a family of tumors consisting of conventional angiomyolipomas, some clear cell tumors and lymphangiomyomatosis. In the literature, there are cases between 9 and 79 years of age. They may occur in the form of abnormal vaginal bleeding, abdominopelvic pain, uterine rupture and hemoperitoneum. Preliminary data suggest a possible relationship between uterine PEComa and tuberous sclerosis. Tuberous sclerosis is associated with four (9.1%) of 44 cases seen in the literature. Histopathologically, it is divided into three groups as benign, malignant and indeterminate malignant potential group. Our aim is to contribute to the sharing of knowledge in the treatment and follow-up management of rare cases of PEComa by risk category.

Case: A 48-year-old female patient was admitted to our clinic with the diagnosis of uterine PEComa after a surgical procedure (TAH + BSO) due to the complaint of vaginal bleeding for two months. Histopathological examination revealed a group of cells with central nuclei with a marked cell boundary located around the thin capillary vascular network. PEComa was divided into three prognostic groups according to histological characteristics. Prognostic markers include size (>5 cm), hypercellularity, marked nuclear atypia, mitotic activity (>1/10 BBA), coagulative tumor necrosis, invasive growth and lymphovascular invasion. In our case; mitosis 2/10 BBA, invasive growth and hypercellularity were observed. Observing two or more prognostic markers is in the high risk category in terms of showing aggressive behavior.

Results: Desmin (+), HMB-45 (+), Melan-A (+), P53 (+), SMA (+) Pathological diagnosis: PEComa

Conclusion: Active follow-up was planned in the patient who had no recurrence or residual findings on postoperative imaging. No recurrence or metastasis has occurred in her follow-ups yet. According to the general view, all patients diagnosed with uterine PEComa need long-term follow-up irrespective of their pathological characteristics until more cases are defined and prognostic criteria become clearer because these neoplasms have an unpredictable natural element.

Keywords: HMB-45, perivascular epithelioid cell, PEComa

ANTIBODY	%
HMB-45	100
Smooth muscle actin	73
Vimentin	56
Desmin	49
Muscle-specific actin	36
CD10	25
Melan-A	24

Table 1.	Immunophenotypic	profile	de-
scribed in	uterine PEComas		



Angiosarcoma Secondary to Radiotherapy Following Breast Surgery: Case Report

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Introduction: Angiosarcoma is a rare tumor originating from vascular endothelial tissue. The breast tissue involvement rate of the tumor observed at the rate of 1% in soft tissue sarcomas reaches up to 8%. Angiosarcoma in the breast tissue is divided into two groups as primary and secondary. Radiotherapy-induced angiosarcoma is a known late complication of radiotherapy after breast conserving surgery. This radiotherapy-induced tumor has a poor prognosis and the 5-year survival rate varies between 10-55%, while the local recurrence rate is reported to reach up to 92%. Radiotherapy-induced angiosarcomas are seen as tumor types difficult to treat due to aggressive clinical course and long, latent process. For this reason, clinicians should be aware of the possibility of angiosarcoma in the case of radiotherapy-induced painless vascular lesions in patients receiving breast conserving therapy.

Case: A 55-year-old female patient underwent breast conserving surgery for a palpable mass in her left breast 10 years ago and was diagnosed with invasive ductal carcinoma (ER +, PR +, Cerb B2 -, T1N0M0). During this period, adjuvant radiotherapy was applied, and the patient was followed up in remission with hormone therapy for five years. The patient was referred to breast surgery because of a palpable mass again. Histopathological examination of the patient operated with negative surgical margin revealed angiosarcoma. The patient is still followed up in remission and there is no evidence of recurrence or metastasis.

Results: CD34 AND CD31 (+), SMA (+), Pancytokeratin (-), HHV8 (-), Ki67 40%. Diagnosis: Angiosarcoma.

Conclusion: In the treatment of early stage breast cancer cases, radiotherapy applied in addition to breast conserving surgery can achieve efficacy equivalent to mastectomy. However, radiotherapy applied after breast conserving surgery also causes an increased risk for the development of secondary angiosarcoma in the late period. Angiosarcoma, about which being an aggressive tumor due to its character should not be forgotten, emerges with clinically painless, red nodule or macular lesions in patients receiving radiotherapy after breast conserving surgery and should be confirmed by biopsy in the early period.

Keywords: Angiosarcoma, breast conserving surgery, radiotherapy



Liver Metastatic Uveal Melanoma Patient with Long-Term Complete Response: Case Report

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Objective: Uveal melanoma is the most common primary malignant tumor of the eye in adults. It is estimated that uveal melanoma is seen in 4.9 men per million and 3.7 women per million. Uveal melanoma has a high tendency to metastasize and it metastasizes to liver (89%), lung (29%) and bone (17%), in order of frequency. Median overall survival time after metastasis ranged from 6 months to 12 months. We aimed to present our case with liver metastasis at the time of diagnosis and followed up and treated for three years with complete response.

Results: A 42-year-old male patient underwent gamma knife treatment in an external center in 2000, who was reported to have a mass behind his right eye. No pathological sampling was performed before. Then, in June 2016, enucleation was performed due to discharge in the right eye. It was reported as phthisic eye with residual necrobiotic spindle cell melanoma focus. The patient was referred to us for treatment and follow-up. The patient's BRAF result was reported as wild-type. First, PET/CT, orbital and brain MR screenings of the patient were performed. No prominent recurrence or lesion consistent with metastasis was detected. Temozolomide at a dose of 150 mg/m² was started to the patient for adjuvant treatment on the 1st and 5th days, with a 23-day break. PET-CT was performed again in the third month follow-up. PET/CT was reported to be stable except for the lesion whose FDG uptake significantly regressed in segment 4A of the liver compared to the previous one. However, because PET/CT which was performed at the time of diagnosis did not mention this lesion, abdominal MR was requested. The patient was referred to general surgery for metastasectomy following the results of abdomimal MRI consistent with PET/CT. Metastasectomy was reported as malignant melanoma metastasis. 4 cycles of ipilimumab treatment was given to the patient after metastasectomy. Subsequently, maintenance treatment was started with temozolomide treatment, to which we had previously received response. The patient is in the 3rd year after diagnosis and there is no recurrence or lesion consistent with metastasis in his scans.

Conclusion: We think that long-term treatment responses can be achieved with multidisciplinary approach and optimal treatment choices in this poor prognostic group of cancer, in which appropriate treatment approaches have not yet been fully clarified due to its rareness.

Keywords: Ipilimumab, uveal melanoma, temozolomide



Case Report: A Case of Regorafenib-Induced Acute Pancreatitis in a Patient with Colon Cancer

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Introduction: Acute pancreatitis is a very common diagnosis. Gallstones and alcohol are the most common causes of pancreatitis, accounting for 75% of cases, but drugs may also cause pancreatitis. Acute pancreatitis induced by regorafenib, an oral, multiple tyrosine kinase inhibitor, used in the treatment of many tumors such as colon cancer, has been reported as a rare side effect. Herein, we reported a case of acute pancreatitis due to regorafenib.

Case: A 71-year-old male patient was diagnosed with colon cancer in 2017. He was operated and received adjuvant KAPOX treatment. In 2018, progression was observed with lung metastasis. After 6 cycles of Folfiri-cetuximab, the disease progressed and capecitabine-bevacizumab was started because of intense neuropathy. Regorafenib was started in July 2019 upon the progression after 3 cycles. The patient who had started to use regorafenib admitted to the emergency department with the complaints of abdominal pain and nausea on the second day of treatment. The patient's pain was spreading to the back. The patient whose examinations performed in the emergency department revealed lipase and anylase elevation (Lipase: 732 u/l, amylase 593 u/l) was hospitalized to the service with a preliminary diagnosis of acute pancreatitis. The patient underwent dynamic abdominal CT: a slight increase in thickness in a limited area of the tail of the pancreas, increased attenuation of the surrounding mesenteric tissue (consistent with pancreatitis).

The patient had no drugs used other than regorafenib, had no hyperlipidemia, and had no history of alcohol use. MRCP was planned. In MRCP, there was no pathology to form filling defect or external compression in the choledochal lumen and intrahepatic bile ducts. The patient was evaluated by gastroenterology as having drug-associated pancreatitis. Lipase values decreased by 43 u/l on the 3rd day of hospitalization. The patient does not have any symptoms at the present time and is being followed up without treatment.

Discussion: Hyperamylasemia is a known side effect due to TKIs and regorafenib. In our case, the diagnosis of pancreatitis was definite with a lipase level greater than three times the upper limit of normal, acute onset abdominal pain and CT findings meeting the diagnostic criteria for pancreatitis. The patient had no known risk factors for pancreatitis and there was a rapid decrease in lipase levels after discontinuation of the treatment.

We wanted to present regorafenib-induced acute pancreatitis because it is rarely seen. This serious side effect should be kept in mind in patients using regorafenib.

Keywords: Acute pancreatitis, hyperamylasemia, regorafenib



Atypical Course in SCLC Patient

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Small cell lung cancer (SCLC) is a disease that responds well to treatment but has a high mortality and in which the chances of long-term survival are not much. Most of the cases are lost due to recurrences, second primary tumors in the late period and non-cancerous causes. It is considered to be a systemic disease due to being at extensive disease stage at the time of diagnosis, distant organ metastasis and regional lymph node involvement. Paraneoplastic syndromes are diseases that occur due to the effect of many biological substances, regardless of the direct invasion and metastases of the tumor. Paraneoplastic syndrome is seen at high rates in SCLC. The case was a 62-year-old male patient with advanced small cell lung carcinoma. He was hospitalized due to neutropenic fever that developed during radiotherapy following three cycles of cisplatin/etoposide chemotherapy. The patient, who recovered from neutropenia after 4 days of follow-up with antibiotic and granulocyte colony stimulating factor (G-CSF) and was planned to be discharged, woke up with acute monoarthritis of his left knee in the morning. Arthritis of the patient was evaluated as inflammatory arthritis. It showed a tendency to clinically regress with antiinflammatory treatment. It was learned that the patient used to have rheumatic joint disease in his history of rheumatologic disease. It was also learned that the patient continued the treatment with Pegfilgrastim and Filgrastim after hospitalization until recovering from neutropenia. No new pathology was detected in the brain imaging of the patient with acute, distal motor deficit two days later. Although it was planned to take cerebrospinal fluid from the patient who was suspected to have Guillain-Barre syndrome, the procedure could not be performed because the patient developed respiratory failure and was then intubated. The patient died due to respiratory failure during intensive care follow-up. Inflammatory monoarthritis of the patient was thought to occur after the activation of the underlying rheumatologic disease via neutrophils following long- and short-acting G-CSF. Although acute motor deficit suggested Guillain-Barre syndrome which can be seen in small cell lung cancer because it primarily affected the distal extremity, unfortunately, its diagnosis could not be finalized. Brain imaging of the patient, who was initially suspected of having Guillain-Barre syndrome and was scheduled for a sample of cerebrospinal fluid, was requested before. The patient whose brain imaging was observed as normal died due to progressive respiratory failure.

Keywords: GCSF, G. Barre, SCLC



Rare Carcinoma of the Breast: Case Report of Sebaceous Carcinoma

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Introduction: Sebaceous differentiation in breast cancer is a very rare condition. To date, approximately 20 cases have been reported in the literature. The World Health Organization defines primary sebaceous carcinoma of the breast as the presence of sebaceous differentiation in at least 50% of the cells in the absence of evidence that it originates from the skin and its supplements. Due to its rareness, little is known about the clinical course and prognosis of this type of breast cancer. In this case, we aimed to discuss the clinicopathologic features and prognosis of sebaceous carcinoma of the breast.

Case: A 39-year-old female patient was admitted to our hospital due to a growing, catarrhal and bleeding lesion on her right breast skin. The patient underwent mastectomy and axillary dissection. Macroscopically, a tumor measured as 15*14*13 cm in size and covering the entire breast was observed. Breast skin was partly ulcerated and irregular. Twenty-two lymph nodes were dissected from the right axilla and 8 lymph nodes were involved. Immunohistochemical examination revealed ER (-), PR (-), HER 2 (-). Ki-67 proliferation index was 10% and histologic grade was 2. PET/CT examination revealed multiple lytic bone metastases but no visceral metastases. The patient was started on palliative radiotherapy and denosumumab 120 mg every 28 days for bone metastases. After palliative radiotherapy, docetaxel 75 mg/m² and capecitabine 950 mg/m² D1-14 were planned to be administered every 21 days.

Discussion and Conclusion: Sebaceous gland cancer is rare. It is often seen in the eyelids and is associated with Muir-Torre syndrome caused by mutations in the DNA damage genes that lead to the loss of expression of specific DNA damage proteins. In most of the cases reported so far, ER/PR is detected as positive, whereas HER2 amplification is very rarely seen. In this case, HER2 was detected as negative in accordance with the literature, and unlike most cases, the hormone receptor was negative. Chen Heng et al. concluded that sebaceous carcinoma of the breast has low invasiveness and good prognosis, but more cases are needed to better define the clinicopathological and prognostic features of this particular type of breast cancer.

Keywords: Breast, pathology, sebaceous carcinoma



A Case of Systemic Metastatic Glioblastoma Multiforme

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Introduction: Glioblastoma multiforme (GBM) is the most common tumor of the central nervous system, originating from astrocytes in adults. With locally aggressive, typical infiltrative character, its local relapse often results in poor prognosis. It is more common in men and its incidence increases with age. Extracranial metastasis of GBM is very rare (<2%). We aimed to present our case who were admitted with systemic metastases because of its rareness.

Case: A 26-year-old female patient underwent chemoradiotherapy and temozolomide treatment following surgery in an external center due to GBM in 2015. During follow-up, a mass lesion in the left lung, hilar and mediastinal conglomerated lymphadenopathy were observed in thorax CT performed due to cough started 4 months ago and PET-CT was recommended to the patient. In February 2019, PET/CT performed in the external center revealed central necrotic metastatic lesions in right axillary, L2 vertebra and lateral of the right arm, medial of the left thigh and muscle plans adjacent to right fibula in the skeletal system in addition to the areas in thorax CT. The patient, whose result of the biopsy taken from the right axillary region was reported as consistent with GBM metastasis in the external center and cranial MRI performed in the external center in March 2019 revealed no recurrence other than postoperative changes, was admitted to our outpatient clinic for systemic treatment. Revision was requested because GBM metastatic presentation from pathology blocks was very rare. Meanwhile, it was also evaluated multidisciplinary at the tumor council. Endobronchial USG (EBUS) was recommended for conglomerated mediastinal lymphadenopathies and differential diagnosis. Right axillary revision blocks and the results of the biopsy taken with EBUS were again reported to be consistent with GBM metastasis. Irinotecan-bevacizumab treatment was started to the patient with the diagnosis of metastatic GBM. No recurrence was observed in cranial MRI for response evaluation after six administrations, whereas PET-CT was requested on mixed response in thorax-abdomen CT. PET-CT revealed lesions in both lungs, mediastinal lymphadenopathies, and dimensional and metabolic progression in skeletal lesions and newly developed interaortocaval lymphadenopathies in the abdomen. It was evaluated as progression and temozolomide treatment was started.

Conclusion: The reason for the rare occurrence of systemic metastases in patients with GBM is unknown. Some authors argue that due to the short survival time of patients with GBM, the disease does not have sufficient time to spread systemically, while others argue that metastases could not be clinically detected.

Keywords: Glioblastoma multiforme, rare, metastatic GBM



A Case of Renal Cell Carcinoma with Right Atrial Tumor Thrombus

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Introduction: Renal cell cancer (RCC) accounts for 3.8% of all adult malignancies and has a high mortality rate. The incidence of tumor thrombus in the inferior vena cava (IVC) has been reported at the rates of 4-10%. We reported a 61-year-old male patient with left renal tumor in which tumor thrombus extends to the right atrium.

Case: A 61-year-old male patient was admitted to the cardiology outpatient clinic with the complaints of fatigue and dyspnea which started one month ago. Physical examination by palpation revealed a solid, fixed, painful mass of approximately 10 cm in the left upper quadrant of the abdomen. Echocardiography showed a multilobulated mass extending from the inferior vena cava to the right atrium. Upper abdominal ultrasonography revealed a heterogeneous solid mass covering the entire right kidney and forming thrombus in the renal vein and IVC. Mediastinal multiple LAPs with the largest one measured 22x9 mm in size and filling defect of tumor thrombus measured 42x31 mm in size filling the right atrium and showing continuity along the inferior vena cava were observed in thoracic and abdominopelvic computed tomography. In addition, a giant mass extending from the renal vein to the superior right atrium and to the inferior right iliac vascularity in the inferior vena cava. The patient underwent right atrial mass excision by CVS, followed by radical nephrectomy and thrombectomy 3 weeks later. The pathology results of the operation specimens were reported as papillary type RCC and there was no tumor invasion at surgical margins. The case was considered as stage pT3C and consulted to our medical oncology clinic. The patient underwent mediastinal lymph node sampling and endobronchial USG. When they were reported as RCC metastasis, interferon (IFN) treatment was started. After IFN treatment, sunitinib treatment was started to the patient with clinically progressive disease.

Conclusion: Treatment-free survival is 5 months on average in RCC patients with IVC thrombus. RCC is resistant to non-operative treatment modalities such as radiotherapy and chemotherapy, and surgery is known to contribute to survival in metastatic patients with good prognostic features. Thrombuses at infra-hepatic level can be removed by abdominal approach. However, surgery is complicated and requires careful planning in renal cell carcinoma patients with suprahepatic or right atrium tumor thrombus.

Keywords: Atrial thrombus, renal cell carcinoma, vena cava thrombus



Primary Pleural Synovial Sarcoma: Due to a Rare Case

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Introduction: Synovial sarcoma accounts for approximately 5-10% of all soft tissue sarcomas. It is often seen as a soft tissue tumor in the extremities of young adults. In the literature, synovial sarcoma in the chest wall and pleura has been rarely reported. Although radiological images are not specific, it should be considered in the differential diagnosis in thoracic masses. Multimodality treatment in the treatment of tumor consists of surgical resection, chemotherapy and radiotherapy. Since the spread of the tumor is very rapid, aggressive surgical resection should be performed as soon as it is diagnosed.

Case: In thorax CT of a 62-year-old female patient who was referred to our hospital on detection of a mass in the lung in the examinations performed in the center she applied with the complaint of dyspnea, appearance of a very large hypodense mass of approximately 100x82 mm in diameter in the left central hilar section extending from inferior lingular segment to superior lower lobe segment, coarse pleural parenchymal band-like atelectasis accompanied by lamellar pleural effusion in the lateral side adjacent to the consolidated area and several satellite nodular densities with the largest one measured as 1 cm in diameter in the laterobasal segment of the left lobe with adhesions were observed. The left lung tru-cut biopsy performed for diagnosis was reported as synovial sarcoma. Pleural fluid sampling was reported as benign cytology. The patient was evaluated as inop by thoracic surgery and she was referred to the oncology outpatient clinic. Ifosfamide + doxorubicin chemotherapy was planned for the patient with the diagnosis of pleural synovial sarcoma, but when hypertensive pulmonary edema developed during the first cycle, the treatment of the patient was changed to doxorubicin as a single agent.

Conclusion: Primary pleural synovial sarcoma is a very rare tumor. It is frequently confused with tumors containing epithelial and mesenchymal components, especially malignant mesothelioma. Immunohistochemical and cytogenetic studies are important in differential diagnosis.

Keywords: Lung, poor prognosis, snovial sarcoma



An Open-Label, Multinational, Multicenter, Phase III Study Evaluating Patient Satisfaction in Subcutaneous Trastuzumab Administration in Patients with HER2 Positive Early Stage Breast Cancer

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Objective: Phase IIIb, multinational, multicenter ML28851 study was designed to evaluate the safety and tolerability of trastuzumab administered subcutaneously (SC) in patients with HER2 (Human Epidermal Growth Factor Receptor 2) positive early stage breast cancer (eBC) and to investigate the treatment satisfaction of patients and health professionals (PHP).

Material-Method: 174 of 223 patients whose consents were obtained and who were screened met the study criteria and their treatments were started. One patient did not receive study medication because the patient did not meet the inclusion criteria. At least one dose of SC trastuzumab was administered to 173 patients with eBC. The primary effectiveness assessment criterion of the study was patient satisfaction measured by questionnaire.

Results: Patient responses (n=170) for SC trastuzumab treatment indicated that most patients (n=166, 97.6%) found the treatment experience satisfactory and 2.4% found it unsatisfactory. Patients and PHPs reported that SC trastuzumab administration was easier (93.5% and 62.5%, respectively). PHPs (n=16; 100%) defined the SC treatment experience as satisfactory. Progression, disease recurrence and death were reported in 24 patients. The 4-year disease-free survival (DFS) and overall survival (OS) rates were 84.2% (\pm 3.1) and 90.5% (\pm 4.7), respectively. The most common adverse event (AE) reported in 34 patients during the treatment period was arthralgia (n=54, 4.2%), influenza (n=41, 3.2%) and nausea (n=39, 3.0%). According to the system organ class, the most common AEs are classified as general disorders and site-related conditions (n=178); these were followed by musculoskeletal system, connective tissue problems (n=166) and gastrointestinal problems (n=149). In the study, 54 cardiac events including left ventricular dysfunction, left ventricular failure and cardiotoxicity were reported. The most common treatment-related AEs were reduction in ejection fraction (EF) (5.4%), erythema (5.0%), pain (5.0%), and rash (5.0%) at the injection site. No treatment was discontinued due to decrease in EF. The decrease in median EF was found as 3.5% (0.12-19.0).

Conclusions: The results of the study showed that SC trastuzumab was favored by patients and PHPs in the treatment of HER2 positive eBC. The safety and tolerability of SC trastuzumab is consistent with the known safety profile of SC and IV administration.

Keywords: Breast cancer, HER 2, subcutaneous trastuzumab, treatment satisfaction



Stage 3 Non-Small Cell Lung Carcinoma with Long-Term Response to Immunotherapy: Case Report

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Introduction: Lung cancer is the leading cause of cancer-related deaths. More than 80 percent of lung cancers are classified as non-small cell lung cancer. Treatment modalities have been developed for epidermal growth factor receptor [EGFR] -mutant, anaplastic lymphoma kinase [ALK] - rearrangement, and ROS1 gene rearrangement. Targeted treatments are ineffective in patients without this genetic factor. Immunotherapy increases survival and improves quality of life in this patient group. We aimed to present a case of stage 3 squamous cell lung carcinoma with long-term response to immunotherapy.

Case: Bronchoscopic biopsy pathology of a 56-year-old male patient in March 2013 was consistent with squamous cell lung carcinoma. Concurrent PET-CT showed mediastinal lymph node involvement (T4N3M0). No metastasis was detected in brain MRI. EGFR/ALK/ROS1 was wild-type. Cisplatin + docetaxel protocol was started to the patient. Mediastinal lymph node progression was detected after 6 cycles of administration. Definitive radiotherapy was applied to primary tumor and mediastinum. Then, 6 cycles of cisplatin + docetaxel protocol was given again. The evaluation revealed a growth in primary mass size. Gemcitabine treatment was started. After 3 cycles, he received vinorelbine protocol due to progression. After three cycles of chemotherapy, liver and bone metastases developed in PET-CT. Single agent nivolumab was started from the early access program. Zoledronate was added to the treatment. After 3 months of administration, liver metastasis disappeared, and primary mass and bone metastases regressed. Radiotherapy was applied to the bone metastasis site. Since September 2015, nivolumab treatment has been applied to the patient. Local treatments have been given to bone lesions, where necessary. There were no complications related to immunotherapy. In the last PET-CT, the disease is stable with mild SUV involvement in primary mass and regressed bone metastasis findings.

Discussion: Although immunotherapy is recommended in first-line treatment of EGFR/ALK/ROS1 wild type advanced lung cancer, most patients receive platinum-based chemotherapy in first-line treatment. Immunotherapy is recommended instead of single agent chemotherapy in second-line treatment. The patient, who had stage 3 squamous cell lung carcinoma and received 3 cycles of chemotherapy before, had PFS for 36 months under single agent nivolumab treatment. The long-term response we got shows that immunotherapy is an efficient treatment in proper patients with advanced non-small cell EGFR/ALK/ROS1 wild-type lung cancer.

Keywords: Chemotherapy, immunotherapy, non-small cell lung cancer



Experience of Trastuzumab-Pertuzumab in a Male Patient with HER2 Positive Metastatic Breast Cancer

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Introduction: Male breast cancer accounts for less than 1% of male cancers. It is detected at a later stage compared to female breast cancers and is mostly low-grade and hormone receptor-positive. HER2 positivity is low. There is little information about the use of HER2 blockade in male breast cancer. We wanted to present the docetaxel-trastuzumab-pertuzumab experience in a male patient with HER2 positive metastatic breast cancer, who was followed up in our medical oncology clinic, because it is a rare case.

Case: A 64-year-old male patient was admitted to an external center with palpable swelling in the right axilla. Superficial ultrasonography revealed 4-5 pathological lymphadenopathies with the largest one measured 52*26 mm in size in the right axilla. The patient underwent thorax and abdomen CT. Multiple lymphadenopathies in the right axillary region with the largest one measured 46*26 mm in size, mediastinal lymph nodes and a 27*18 mm lesion in the left adrenal gland were observed. The patient underwent tru-cut biopsy of the axillary lesion in the external center. The pathology was consistent with malignant epithelial tumor. The patient was admitted to our clinic with these findings. His physical examination revealed a palpable, fixed and solid mass measured approximately 55*50 mm in the right axilla. No palpable mass was detected in bilateral breasts. PET/ CT revealed multiple right axillary and pectoral hypermetabolic lymph nodes with the largest one measured 40*35 mm in size, some of them were conglomerated, mediastinal hypermetabolic lymph nodes, hypermetabolic soft tissue lesions in the lower lobes of both lungs, and left adrenal hypermetabolic lesion.

In the pathological consultation, it was evaluated as malignant epithelial tumor, ER and PR negative, cerbB2 +3, and most probably breast carcinoma.

Docetaxel-Trastuzumab-Pertuzumab treatment was started. PET/CT taken at the end of 3 cycles of treatment showed regression in size, number and activity in right axillary and mediastinal lymph nodes and previously detected lesion in the left gland was not observed. The patient who is responsive to treatment continues treatment.

Discussion: HER2 positivity is very rare in patients with male breast cancer. Because of the small number of cases, it is difficult to conduct clinical studies. Information on this subject is obtained from case reports. We wanted to share this case with the thought that it will contribute to the literature because it is a rare case and we use HER2 dual blockade.

Keywords: Breast cancer, HER2 positive, male patient, pertuzumab, trastuzumab



Nearly Complete Respone With First-Line Atezolizumab + Carboplatin + Etoposide in a Case with Metastatic Small Cell Neuroendocrine Lung Carcinoma

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Objective: Since the 1980s, concurrent CRT in limited disease, PCI in responsive patients and first-line platinum etoposide combination at all stages are recommended as standard treatment of SCLC. The median survival time is 20 months in limited diseases and 10 months in extensive diseases with these treatments. Improvements in SCLC treatment were limited for a long time. However, in recent years, as in other cancer types, immunotherapy studies have been accelerated in SCLC treatment as well. In the IMpower 133 study, it was shown that first-line atezolizumab+EP combination provided better survival compared to EP combination alone in extensive-disease SCLC. This was the first combination of immunotherapy + chemotherapy, which provided survival advantage in the first-line treatment after EP combination that is the standard treatment regimen. Herein, we presented a case with nearly complete response with this combination.

Results: A 63-year-old male patient admitted to us in March 2019 was diagnosed with SCLC by EBUS. In PET-CT performed for staging purposes, primary mass in the right lung, multiple metastatic lymph nodes in the cervical region, mediastinum and abdomen and metastatic nodules in both adrenals were detected. There was no metastasis in brain MRI. First-line atezolizumab+EP was started to the patient with the diagnosis of extensive-disease SCLC. After 4 cycles, PET-CT showed a nearly complete response in all lesions (Fig. 1). No side effects related to treatment were observed. He is receiving maintenance treatment with atezolizumab right now.

Conclusion: In the IMpower 133 study, 403 patients with newly diagnosed extensive-disease SCLC were randomized into two arms. One arm was given 4 cycles of EP+atezolizumab followed by atezolizumab maintenance, the other arm was given 4 cycles of EP+placebo, followed by placebo maintenance until disease progression or unacceptable toxicity. At a mean follow-up of 13.9 months, ORR and PFS were similar in both arms. (60.2%, 5.3 months atezolizumab, 64.4%, 4.3 months placebo, respectively) Median overall survival was better in the atezolizumab arm. (12.3 months vs. 10.3 months; HR: 0.70) Again, one-year survival rate was better in the atezolizumab arm (51.7% and 38.2%). In 351 out of 403 patients, blood TMB was observed but there was no relationship between TMB and clinical benefit. This is the first study showing a survival advantage for 3 decades. In the treatment of newly diagnosed extensive-disease SCLC, addition of atezolizumab to first- line EP has provided a new standard of treatment.

Keywords: Atezolizumab, immunotherapy, small cell lung cancer

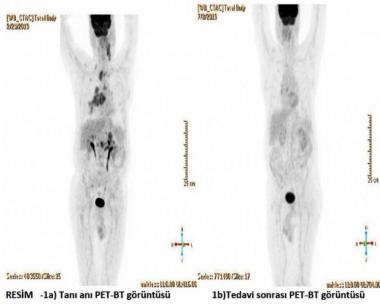


Figure 1. PET-CT images. 1a) PET-CT image at the time of diagnosis 1b) PET-CT image after treatment.



A Case of Atypical RCC Presenting With Bone Metastasis

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Introduction: Renal cell carcinomas (RCC) originate from the renal cortex and account for 80-85% of primary renal tumors. While most of the localized patients are incidentally detected, symptoms depending on the site of metastasis may be seen in metastatic disease. The most important stage in the diagnosis of the disease is pathology. We planned to present an atypical RCC case in this report.

Case: A 47-year-old male patient was admitted to our orthopedic outpatient clinic with the complaints of pain and swelling under his left knee. The patient's history was unremarkable except for 18 pack/year smoking. Physical examination revealed swelling and tactile sensitivity in the proximal part of the left tibia, but no increase in temperature or color change was present. In routine laboratory tests, normochromic normocytic anemia was present and LDH 342 U/L was detected. MR imaging of the left cruris-knee-thigh region revealed a 103*48 mm mass lesion extending from the proximal left tibia to the distal femur. Trucut biopsy of the mass revealed CkPan (+), Vimentin (+), CD-10 (+), Pax-8 (+), CD-34 (-), CD-31 (-), Melan-A (-), TTF-1 (-), CK-7 (-) and CK-20 (-) and the patient was diagnosed with RCC metastasis. There was no additional abnormality in thorax and abdomen CT for primary investigation and possible additional metastases and no space-occupying lesions were found in both kidneys. The patient was operated on without any additional bone involvement on whole body bone scintigraphy. The operation pathology was also consistent with the RCC. The patient was treated with interferon for 1 year in the adjuvant period, followed by untreated follow-up.

Discussion: RCC immunogenicity is one of the most well-known tumor types. Rare cases of primary RCC with diffuse necrosis have been reported in the literature, especially in sarcomatoid type. However, a case of RCC whose primary completely disappeared has not been reported.

Conclusion: RCC is an immunogenic tumor and RCC should be kept in mind in metastatic patients whose primary cannot be detected because primary lesions may disappear in rare untreated cases.

Keywords: Immunogenicity, interferon, renal cell carcinoma



Correlation of Platelet Distribution Width with Stage and Presence of Ras Mutation in Patients with Colon Cancer

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Introduction: Colon cancer is one of the most common types of cancer and stage of the disease is important in prognosis. The presence of RAS mutations may affect the prognosis of the disease and has an important role in the choice of treatment. Platelet indices have recently been studied extensively as a marker of inflammation, suggesting that they may give clues about the level of inflammation. In this study, we aimed to investigate the correlation of platelet distribution width (PDW) with the stage of colon cancer and the presence of RAS mutation.

Material-Method: The medical records of 92 patients who were followed up in the Medical Oncology Policlinic of Kırıkkale University Faculty of Medicine were retrospectively examined. Patients who did not receive chemotherapy and did not have infectious or inflammatory pathologies were included. Patients with and without RAS mutation were divided into two groups and their hemogram parameters, especially PDW values, were compared. PDW values were compared according to the stage of the patients. Correlation between stage and PDW was evaluated.

Results: The mean age of the patients was 66.1 ± 14.4 years; 61 of the patients were men and 31 were women. There were 11 patients at stage 1, 20 patients at stage 2, 20 patients at stage 3, and 41 patients at stage 4. 88 patients had RAS mutation. Of these, 49 were negative and 38 were positive. There was no significant difference between two groups with positive and negative RAS mutation in terms of PDW (15.9 ± 0.9 vs 16.1 ± 0.6 , respectively, p=0.14). According to the Kruskal-Wallis test, PDW values were significantly different between the four stages (p=0.003). There was a significant positive correlation between stage and PDW with low correlation coefficient (r=0.35; p=0.01).

Conclusion: In this study, PDW increased as the stage increased, but no correlation was found between RAS mutation and PDW. This may be associated with an increase in the level of inflammation as the stage increases. More extensive studies are needed on this subject.

Keywords: Colon cancer, PDW, RAS mutation



A Case of Renal Cell Carcinoma Metastasizing to Anterior Abdominal Wall 13 Years After Nephrectomy

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A 73-year-old male patient underwent nephrectomy for left renal carcinoma in December 1995. Pathology was reported as renal cell carcinoma (grade 2) (left renal) Renal cell carcinoma metastasis (left adrenal). The patient did not receive chemotherapy or radiotherapy. He received only interferon treatment for 1 year.

Results: The patient presented again with mass in the upper half of the abdomen in April 2008. Abdominal CT performed with a preliminary diagnosis of abdominal hernia revealed two contrasted, adjacent solid mass lesions in right upper half of the anterior abdominal wall in the skin-subcutaneous tissues with the larger one measured approximately 3.5 cm in diameter. Two well-circumscribed nodular lesions adjacent to the pancreas process and tail, which were highly contrasted compared to the pancreas parenchyma, with the larger one measured 15*13 mm in size, and which were not separated clearly from the pancreas were observed. On being reported as (metastasis?), biopsy was taken from the mass in the anterior abdominal wall (May 2008). The pathology was reported as clear cell carcinoma metastasis. Sunitinib malate at the dose of 50 mg/day was started to the patient with the diagnosis of metastatic renal cell carcinoma. At the end of the second month, the drug was stopped due to general condition disorder (nausea, vomiting, weight loss, neutropenia, malaise, fatigue, jaundice, thyroid function disorder).

Keywords: Metastasis, renal cell carcinoma, sunitinib malate



Activity of C61, a SYK Tyrosine Kinase Inhibitor, in Prostate Cancer

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Introduction: Prostate cancer, the most common type of cancer among men, is the second leading cause of cancer-related deaths. Metastatic castration-resistant prostate cancer (CRPC) has a poor prognosis. Therefore, therapeutic innovations are needed. Spleen tyrosine kinase (SYK) has emerged as a new molecular target for CRPC. SYK plays the main regulator role in many signaling pathways. In this study, the cytotoxicity of C61-LNP, a potent SYK inhibitor, to human prostate cancer (PC-3) cell lines was investigated.

Material-Method: Various concentrations of C61-LNP and cisplatin were administered alone or in combination to PC-3 cells for 24, 48 and 72 hours. Cell viability was evaluated by MTS test. Cellular expression levels of various regulatory proteins in cells exposed to these agents were evaluated by Western blot.

Results: C61-LNP shows dose-dependent cytotoxicity against PC-3 cells (Fig. 1). The levels of caspase 3 and 9, which are thought to be involved in the realization of apoptosis in response to different stimuli in prostate cancer cells, are significantly increased in the group treated separately with C61-LNP and cisplatin compared to the control group (p<0.001). However, the highest caspase 3 and 9 levels were obtained in the combination arm (p<0.001). This data shows that cisplatin inhibits apoptosis in PC-3 cells by caspase pathway. In addition, when C61-LNP was administered alone or in combination with cisplatin, it causes an increase in Bax protein inducing apoptosis (p<0.001) and a decrease in Bcl-2 protein inhibiting apoptosis (p<0.001). With the administration of C53-LNP and cisplatin alone or in combination, statistically significant changes were observed, in PC-3 cells, in the levels of p53, p21, p27, cyclin D1 and cyclin E, which are cell cycle regulatory proteins compared to the control group (p<0.001).

Conclusion: C61-LNP exerts its anti-cancer effect on PC-3 cells by regulating cell cycle in G1 phase and increasing apoptosis. It ensures apoptosis with activation of caspase 3 and 9, increased bax protein and decreased Bcl-2 level. Our study demonstrates that C61-LNP can be used as a part of the multi-modality treatment strategy for CRPC.

Keywords: Apoptosis, C61-LNP, cell cycle, prostate cancer

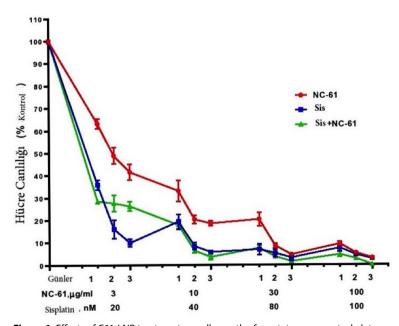


Figure 1. Effects of C61-LNP treatment on cell growth of prostate cancer cytoskeletons. The data are represented as the relative cell viability of the treated cell compared to the control and are shown as the mean±SD of the three independent experiments.



A Case of Lung Adenocarcinoma with Metastasis to the Pancreas

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Introduction: Lung cancer has many metastatic sites, mainly other part of the lung, bone, adrenal and brain. Metastasis to the pancreas has been rarely reported.

Case: Abdominal pain for 1 month occurred in a 62-year-old male patient with 45 pack/year smoking. Laboratory examination revealed leukocytosis, neutrophilia and CEA elevation. CA-19.9 was normal. In the imaging performed for the purpose of malignancy research, CT revealed a 24x22 mm mass lesion at the widest part in apicoposterior upper lobe of the left lung with irregular margins and small cavitation and millimetric nodular lesions in the right and left lungs. In addition, a nodular lesion measured 22x12 mm in size was observed in the head localization of the pancreas. No pathology was detected in the GIS screening. Biopsy was performed to the lesions in the lung and pancreas. Pathology result of the biopsy taken from the pancreas was reported as adenocarcinoma infiltration, CK7 (+), TTF-1 (+), CK20 (-). Tru-cut biopsy of the left lung mass was presented as adenocarcinoma. The patient who had a radiological appearance supporting primary lung tumor and with TTF-1 positive was evaluated as having lung adenocarcinoma with pancreatic metastasis. Cisplatin pemetrexed chemotherapy was started to the patient with ECOG performance status 1. Pemetrexed maintenance treatment was started after 6 cycles of chemotherapy. In the 3rd month of pemetrexed treatment, PET/CT revealed a stable nodule with pathological FDG uptake and spicular extensions in the apicoposterior segment of the left lung. Cyber knife treatment targeting the lesion in the lung was applied to the patient. At 8 months, new lesions developed in both lungs and abdominal midline. A sample was sent from the patient for mutation analysis from peripheric blood. The patient was informed about immunotherapy and docetaxel treatment was started in the second-line treatment.

Conclusion: Pancreatic metastasis is very rare in lung cancer. Malignant melanoma, renal cell cancer, colon, stomach, breast, lung and liver cancers have been shown to metastasize to the pancreas. Lung adenocarcinoma is difficult to differentiate from primary pancreatic adenocarcinoma. Primary tumor and metastasis can be differentiated by clinical evaluation, radiological appearance and histopathological examination. TTF-1 positivity and absence of DPC-4 gene loss are the findings supporting lung adenocarcinoma. In patients with synchronous tumors, biopsy of the lesions is important for diagnosis and treatment of the disease.

Keywords: Lung adenocarcinoma, metastasis, pancreatic adenocarcinoma



A Case of Lung Carcinoma with Good Response to the Combination of Immunotherapy and Chemotherapy

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Introduction: Immunotherapy is accepted as standard treatment in patients with non-small cell lung carcinoma (NSCLC), although it is not within the scope of reimbursement. Especially in patients who we think will respond well to immunotherapy, cost has an impact on the selection of treatment regimens.

Case: The 68-year-old woman was admitted in July 2018 due to a swelling on the left side of the neck, which she had been aware of for three months. She had known hypertension. In routine examinations, chronic disease anemia was observed, sedimentation was 62 mm/h and CEA level was 201. In the USG, biopsy was taken from 1.5 cm LAP with indistinct fatty hilus. Metastasis of poorly differentiated carcinoma was found as consistent with CK 7 (+) CK 20 (-) TTF-1 (+) Napsin A (+) p63 (-) Lung adenocarcinoma. Thorax CT showed a 3.5 cm hypodense mass with circumferential heterogeneous infiltration in the left hilar region, no mediastinal lymph node was observed. Axillary pathological lymph node was detected. No further distant metastasis was detected on abdominal CT. Axillary LN sampling was also consistent with lung adenocarcinoma. Molecular tests were performed as stage 4 lung adenocarcinoma. They were found as EGFR (-), ALK (-), ROS-1 (-) and PDL-1 80%. As appropriate treatment method, immunotherapy options were suggested to the patient. Paclitaxel, Carboplatin and Atezolizumab combination was started due to cost. At the end of 6th cycle, partial response was detected according to RECIST in the imagings of the patient whose CEA level decreased to 10. SBRT was applied to the residual primary hilar mass and axillary metastasis. Atezolizumab continued until March 2019. In the imaging of the clinically asymptomatic and stable patient taken in April, increased bronchoalveolar spread in the lung, progression or infection suspected areas were detected. Atezolizumab was discontinued and antibiotherapy was started. Infiltrations were observed to be stable in CT control one month later. The patient was started on prednol 32mg orally with a preliminary diagnosis of pseudoprogression. After 15 days, a significant decrease in PAAC control was detected and the patient was followed up to deescalate prednol treatment.

Conclusion: Overall survival in SCLCs is reported to be 9-11 months for advanced stage disease. Survival time reaches 20 months with Pembrolizumab and Atezolizumab. In the first series, only Pembrolizumab can be used as a single agent. Reimbursement problems limit the use of Pembrolizumab in eligible patients. The IMPOWER-150 study can be considered as a basis for adding Atezolizumab to our chemotherapy regimens.

Keywords: Immunotherapy, non-small cell lung cancer, pseudoprogression

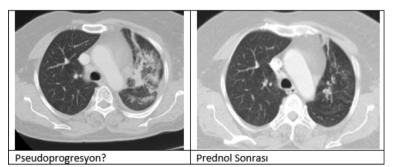


Figure 1. Progression?

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A Case of Myelitis Due to Immune CheckPoint Inhibitor

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Introduction: With the recent advances in understanding the regulatory mechanisms of the immune system, agents targeting cytotoxic lymphocyte-associated protein 4 (CTLA-4) and programmed cell death-1 (PD-1) have begun to be used in oncology today. Anti-PD1/PD-L1 antibodies target the PD-1 checkpoint protein on the surface of active T cells. Disease-free survival and overall survival times are shown in nivolumab versus PD-1 in RCC. The most common side effects of nivolumab are rash, colitis, hepatitis, endocrinopathies, and pneumonia. Neurological side effects are rare but include immune polyneuropathies, Guillain Barré syndrome, myasthenia gravis, posterior reversible encephalopathy syndrome, aseptic meningitis, enteric neuropathy, transverse myelitis, and immune encephalitis cases.

In this case report, we presented a case of transverse myelitis due to the use of nivolumab, an immune checkpoint inhibitor..

Case: A 70-year-old male patient received nivolumab treatment in June 2018 due to progressive disease following the treatment of IFN and pazopanib with the diagnosis of metastatic renal cell cancer in 2016 and he was admitted to our hospital with loss of strength and numbness in the lower extremities after the 10th administration of nivolumab treatment. The patient was consulted to the neurology department. Physical examination of the patient revealed a 4/4 loss of strength in bilateral lower extremities. Cranial MR, thoracolumbar MR, lumbar puncture and EMG were performed. There was no septic finding as a result of lumbar puncture. Cytological examination of Lp was acellular. No abnormalities were detected in MRI results. Sensorineural axonal neuropathy was detected in EMG. It was thought to be transverse myelitis by the current clinic of the patient and the neurology department. Methylprednisolone at a dose of 1 mg/kg was started rapidly. On the 5th day of treatment, motor functions of the patient improved. In the follow-ups, the patient's loss of strength and sensation regressed and steroid treatment was continued for 1 month. Steroid treatment was gradually decreased and discontinued in the follow-ups. The loss of strength in the lower extremities of our patient disappeared near to total.

Discussion: It is important to rule out seizure activity, infection and metabolic disorder, which may be the underlying causes of neurological deterioration in the use of immune check-point inhibitors used in the treatment. Neurology consultation is recommended in the early period. Depending on the clinical manifestations and imaging of the central nervous system, nerve conduction studies and lumbar puncture may aid in the diagnosis. These patients benefit from steroid treatment.

Keywords: Immune checkpoint inhibitors, nivolumab, transverse myelitis



Donor Cancer Transmission after Renal Transplantation - Case Report

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Objective: Cases with cancer transmission have been reported, although rarely, due to failure to diagnose cancer in the living organ donors at micrometastatic stage. Immunosuppressive agents used to prevent graft rejection may cause cancer to progress faster.

Methods: Three months after living renal transplantation, extensive metastatic disease whose primary was thought to be pancreatic cancer was detected in the donor.

Results: The father of a 21-year-old patient with end-stage renal failure who underwent renal transplantation from his father in December 2018 was found to have extensive metastatic disease whose primary was thought to be pancreatic cancer approximately 3 months after transplantation. Biopsy of the donor's metastasis in the liver was consistent with poorly differentiated adenocarcinoma [TTF-1 weak focal (+), Napsin A (-), CK 7 (+) and CK 19 (+)]. Since the creatinine values of the recipient were high, biopsy was taken from the transplanted kidney and reported as metastasis of poorly differentiated carcinoma. The patient with no evidence of distant metastasis in thorax and abdomen CT underwent emergency nephrectomy. The pathology was consistent with poorly differentiated adenocarcinoma. The tumor was invaded with perinephritic fatty tissue and striated muscle, and the surgical margin was detected as positive. Immunohistochemical examinations had the same characteristics as cancer tissue from the donor. However, PD-L1 expression was different in both tumor tissues, PD-L1 was (-) in the donor while PD-L1 expression was 60% in tumor cells and 10% (+) in tumor-related immune cells in the tumor of the recipient. Targeted mutations, translocations and changes in gene expression of the 26 most commonly reported genes in solid cancers were investigated, and no pathogenic changes were detected. Postoperative PET-CT showed extensive implant in the operation site in the abdomen, and multiple infradiaphragmatic lymph nodes up to 2 cm in diameter. Then, the patient's immunosuppressive treatments were discontinued and gemcitabine-carboplatin was started at renal dose. After three cycles of chemotherapy, which was completed by dose reduction due to sepsis, progressive disease was detected in the performed examinations. The combination of chemotherapy and immunotherapy was planned.

Conclusions: Donor cancer transmission, which is a very rare (2/10.000) condition, may not be detected despite all preoperative examinations. Progression of the cancer is possible even if immunosuppression in the recipient is eliminated. There is no sufficient data on the use of immunotherapy in these patients.

Keywords: Cancer transmission, donor, immunotherapy, transplantation

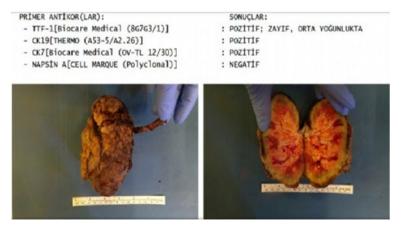


Figure 1. Left nephrectomy material and IHC results.



The Effectiveness of Cetuximab- and Platinum-Based Kt for Recurrent/Metastatic Head and Neck Cancers: Real-Life Data

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Giriş: The prognosis of recurrent and/or metastatic squamous cell head and neck cancers is considered to be poor. Overall survival rate usually varies between 6-12 months depending on patient/disease-related factors. In 2008 the EXTREME study showed that cetuximab treatment with cisplatin-based chemotherapy improves survival rate.

Amac: The aim was to research the demographic and clinical characteristics and the survival rates of the patients with recurrent and/or metastatic squamous cell head and neck cancers who were being treated with the EXTREME regimen, as well as the factors affecting their survival rates.

Tartışma: The EXTREME study showed that adding cetuximab to cisplatin+5 fu treatment makes a positive contribution in survival rate. Our study also yielded similar results with that of the EXTREME study.

Anahtar sözcükler: Cetuximab, head and neck cancers, platinum

TREATMENT RESPONSE				
Response to treatment (After the 3rd chemotherapy)	Full response: 9 (13.2) Partial response: 18 (26.5) Stable disease: 12 (32.4) Progression: 19 (27.9)			
PFS OS	Median: <i>4.9</i> (1.2-26.4) Median: 7.4 (2-52)			

Table 1.



A Case of Gastric Carcinoma in Remission After Liver Metastasectomy: Case Report

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Introduction: Gastric cancer is the fifth most common malignancy and the third leading cause of cancer-related deaths in the world. Although the only curative treatment option is surgery, the role of metastasectomy is controversial in gastric cancer patients with liver metastasis. Our case is a gastric adenocarcinoma patient with long-term survival with liver metastasectomy.

Case: A 63-year-old male patient was admitted to the general surgery clinic with the complaints of nausea, vomiting, and epigastric pain. Upper gastrointestinal system endoscopy revealed an ulcero-vegetative mass in the gastric antrum, biopsy was taken and the pathology was reported as gastric adenocarcinoma. The patient underwent partial gastrectomy, and intraoperative metastasectomy was performed to a focus that was thought to be a possible metastasis in the liver. According to pathology result, liver was consistent with gastric adenocarcinoma metastasis and 1 of 15 removed lymph nodes were reported as positive.

Adjuvant XELOX (capecitabine+oxaliplatin) chemotherapy was planned for the patient, whose systemic screening tests revealed no further distant metastasis, with the diagnosis of T3N1M1 (metastasectomy) operated gastric adenocarcinoma. After 6 cycles, oxaliplatin was discontinued and treatment was continued with maintenance capecitabine. The patient operated in December 2016 is still followed up in remission (33 months) under maintenance treatment as of September 2019.

Conclusion: In the meta-analysis results, the expected 5-year overall survival (OS) was detected as 22-23% in patients with gastric cancer who underwent liver metastasectomy. As in our case, long-term survival can be achieved in patients diagnosed with gastric cancer where both primary tumor and liver metastases can be removed by R0 surgical resection.

Keywords: Gastric cancer, liver metastasis, metastasectomy



EP-037

Synchronous Metastatic Laryngeal Squamous Cell Carcinoma and Lung Adenocarcinoma Case Report

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A 63-year-old male patient were admitted with the complaints of increasing hoarseness and dysphagia for 3 months. Physical examination revealed lymphadenopathy in the right cervical and submandibular areas. After detailed ENT examination and imaging, biopsy of the tumor mass on the epiglottis laryngeal and ventral surface revealed a squamous cell carcinoma consistent with moderate differentiation. In PET/CT performed for staging purposes, 4.5 cm mass extending from the hypopharynx to the supraglottic level and bilateral conglomerated LAPs in the neck, multiple nodules with the largest one measured (27*23 mm in size) in the lower lobe of the right lung, hilar, subcarinal and mediastinal multiple LAPs, right pleural effusion and 16*13 mm nodule with FDG uptake in the localization of segment 7 of right lobe of the liver were detected. The wedge resection of the largest sized nodule in the right lung was consistent with acinar dominant adenocarcinoma, and pleural cytology sampling was evaluated as malignant, while core biopsy of a single nodule in segment 7 of the liver was evaluated as consistent with malignant epithelial tumor metastasis and laryngeal squamous cell carcinoma metastasis after immunohistochemical study.

Platinum+taxol treatment was planned for the patient whose body weight was 40 kg (BSA: 1.4) and ECOG Performance Status was 2-3. Meanwhile, the molecular study was accelerated but epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) and proto-oncogene tyrosine-protein kinase 1 (ROS1) were detected as negative.Intermediate evaluation after 3 cycles of platinum+taxol showed significant regression of primary tumor in the larynx and bilateral neck LAPs; lung-pleural effusion-multiple mediastinal LAPs and liver lesion were consistent with complete metabolic response. In the evaluation after 6 cycles, they were consistent with nearly complete metabolic response.

Significant improvement was observed in the general condition at the last outpatient visit and ECOG score was 1 in the evaluation after the examination. Since the tolerance of CT and CT response were good, 2 more cycles of platinum+taxol treatment were planned. The PD-L1 result is eagerly awaited.

Keywords: Double primary, laryngeal squamous cell carcinoma, lung adenocarcinoma, synchronous

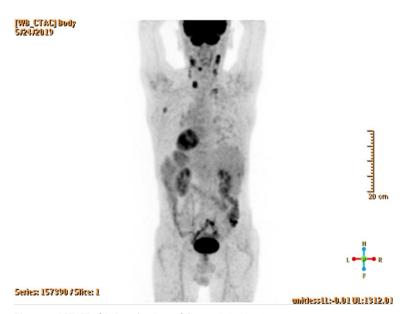


Figure 1. PET/CT of A.C. at the time of diagnosis in May 2019.



Efficacy and Success of AF Ablation in Cancer Patients

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Introduction: With the increased survival of cancer patients, cancer-therapy related cardiovascular disease has become more common and recognized more. Arrhythmia commonly occurs during cancer therapies. Atrial fibrillation is the most common type of chronic arrhythmia in the community, successfully treated with ablation in drug-resistant cases. There is limited data in the literature on the efficacy of AF ablation in cancer patients.

Method: The patients, who underwent AF ablation in Hacettepe University Hospital Cardiology Department in the period from January 2013 and June 2019 were evaluated retrospectively. AF recurrences were investigated comparing the cancer patients in one group and non-cancer patients with a similar age and sex distribution in the other group. Recurrences in the first 3 months after ablation were considered early and later recurrences were considered late. Access site complications included developing a pseudoaneurysm, hematoma, or AV fistula after the procedure.

Results: Twenty-seven cancer patients and 27 non-cancer patients having a similar age and sex distribution were included in the study provided that they underwent AF ablation. The baseline characteristics are presented in Table 1. The median followup period after ablation was 14.5 (6-57) months. Early recurrence and total recurrence were significantly different in patients with malignant disease but this difference was not statistically significant (Table 1). The incidence of access site complications was similar between the two groups (p=1.000). There were no differences in the early, late or total recurrence rates between the solid and hematologic malignant disease groups. Early, late and total recurrence rates were similar between the patients receiving anthracycline therapy and the patients not receiving anthracycline therapy. Total recurrence was significantly more common in the patients receiving radiotherapy and bisphosphonate therapy compared to the control group. It was found out that early relapses were significantly more common in the bisphosphonate receiving patients and late relapses were more common in radiotherapy patients (Table 2).

Discussion: The efficacy of AF ablation in cancer patients is similar to that performed in non-cancer patients. Bisphosphonate use and a history of radiotherapy to the thorax appear to reduce the efficacy of AF ablation. Phrenic nerve injury and local complications do not occur at different rates in cancer and non-cancer patient groups after AF ablation. AF ablation is effective and safe in patients with malignancy.

Keywords: Atrial fibrillation, ablation, cancer

Tumor Type	Solid	Hematologic	p-value
Early recurrence; n (%)	3 (14.2%)	2 (33.3%)	0.303
Late recurrence, n (%)	2 (9.5%)	1 (16.6%)	0.545
Total recurrence, n (%)	5 (23.8%)	3 (50%)	0.319
Type of Chemotherapy	Anthracyclines (Yes)	Anthracyclines (None)	p-value
Early recurrence; n (%)	2 (18.1%)	3 (18.7%)	1.000
Late recurrence, n (%)	2 (18.1%)	1 (6.2%)	0.549
Total recurrence, n (%)	4 (36.3%)	4 (25%)	0.675
Thoracic Radiotherapy	RT Yes	RT None	p-value
Early recurrence; n (%)	2 (25%)	3 (15.7%)	0.616
Late recurrence, n (%)	3 (37.5%)	0 (0%)	0.019*
Total recurrence, n (%)	5 (62.5%)	3 (15.7%)	0.027*
History of bisphosphonate use	Bisphosphonate (Yes)	Bisphosphonate (None)	p-value
Early recurrence; n (%)	4 (57.1%)	1 (5%)	0.009*
Late recurrence, n (%)	2 (28.5%)	1 (5%)	0.156
Total recurrence, n (%)	6 (85.7%)	2 (10%)	0.001 *

Table 1. Basal characteristics and ablation outcomes

Table 2. Factors associated with AF ablation outcomes in cancer patients

	Patients with malignant disease	Control Group	p-value
The number of patients (n)	27	27	
Gender, Male, n (%)	12 (44.4%)	13 (48.1%)	1.000
Age, mean±SD	63.26 ± 10.30	64.30 ± 10.30	0.713
CAD, n (%)	12 (44.4%)	18 (66.6%)	0.100
Hypertension, n (%)	14(51.8%)	19 (70.3%)	0.163
Diabetes, n (%)	14(51.8%)	19 (70.3%)	0.163
LVESD, cm, mean \pm SD	5.04 ± 0.54	4.78 ± 0.763	0.112
LV EF, (%), mean ± SD	58.57 ± 10.57	58.59 ± 10.11	0.995
LA diameter, cm, mean \pm SD	3.98 ± 0.65	3.91 ± 0.51	0.628
Follow-up period, month, median, (min-max)	14 (6-51)	15 (6-57)	0.264
AF recurrence: Early recurrence; n (%) Late recurrence; n (%) Total recurrence; n (%)	5 (18.5%) 3 (11.1%) 8 (29.6%)	1 (3.7%) 2 (7.4%) 3 (11.1%)	0.192 1.000 0.175
Phrenic nerve injury, n (%)	1 (3.7%)	0 (0%)	1.000
Access site complications, n (%)	3 (11.1%)	2 (7.4%)	1.000



Analysis of Tissue Cytokine Levels in Rats with Cisplatin-Induced Experimental Nephrotoxicity

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Objective: Analysis of tissue cytokine levels in rats with cisplatin-induced experimental nephrotoxicity.

Material and Method: Twenty Sprague – Dawley male rats were included in the study and assigned to two groups of 10. The Sham group (Group I) received a single intraperitoneal (ip) dose of 1 cc saline every 12 hours. The cisplatin group (Group II) received a 10 mg/kg ip dose of cisplatin to induce nephrotoxicity (Group II). Each group was placed in a metabolic cage for one week. Saline solution was administered every 12 hours, starting 36 hours before inducing nephrotoxicity with cisplatin. Bodyweight and 24-hour urine of the rats were followed up in the metabolic cage. The rats were anesthetized with a 5 mg/kg dose of rompun and 100 mg/kg dose of ketamine 84 hours after the cisplatin administration; then, they were sacrificed. Then, blood samples were collected from the abdominal aorta and kidney samples were collected to test the levels of tissue antioxidant enzymes. Kidney tissue samples were assigned to two groups. The samples in one group were fixed in formalin and the samples in the other group were fixed in glutaraldehyde. These two groups were separately stored in the refrigerator at -80°C until the time of analysis.

Results: The comparison of Group I and Group II revealed that the levels of urea and creatinine increased significantly (p=0.001 for both parameters), indicating cisplatin-induced nephrotoxicity. Tissue TNF- α levels of Group I and Group II were significantly different (p=0.049); however, there were no significant differences in the tissue levels of IL-1 β , IL-10, and IL-6 (p=0.151, p=1, p=0.545; respectively).

Conclusion: Cisplatin is one of the most important antineoplastic drugs used for treating solid tumors. Nephrotoxicity is the most important dose-limiting side effect. According to the data obtained from this study, a single high dose of cisplatin in cancer therapy causes kidney injury. It is known that inflammation is one of the major mechanisms in cisplatin nephrotoxicity and that TNF- α plays a central role in its development. In the group with cisplatin-induced nephrotoxicity, there has been a significant increase in the tissue levels of TNF- α , which is an inflammatory cytokine. However, there have been no significant changes in the tissue levels of IL-1 β and IL-6, both of which are inflammatory cytokines, too. Also, there has not been an increase in the tissue levels of IL-10, which is an anti-inflammatory cytokine.

Keywords: Cisplatin, cytokine, nephrotoxicity



Integrated Palliative Care Outpatient Clinic: Hacettepe Oncology Hospital's Experience

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Aim: The benefits of integrated palliative care include improvements in symptom control, quality of life, and survival. Palliative care outpatient clinics are either integrated into oncology clinics or organized independently as two different models. An integrated palliative care outpatient clinic model was implemented in our healthcare center 9 months ago. In this paper, we present our first experiences of an integrated palliative care outpatient clinic, which is comprised of a medical oncologist, an internal medicine physician, and an oncology nurse in the Hacettepe University Medical Oncology Clinic.

Methods: Patients referred by an oncologist or patients who were not referred but presented with serious symptoms were admitted to our outpatient clinic. Excluding the patients with acute symptoms requiring emergency interventions; every patient was routinely administered the Edmonton Symptom Assessment Scale (ESAS), Nutritional Risk Screening 2002, and visual analog scale for pain. Besides, their medical histories were taken and they underwent physical examinations at baseline. All kinds of interventions and consultations were documented for every patient.

Result: A total of 174 patients were admitted to our clinic in the first 5 months. The demographic and clinical characteristics of the patients are listed in Table 1. The major complaints of the patients at the time of admission included pain (26%), nausea and vomiting (13%), and impaired oral intake (9%). Additional to the major complaints, the patients had a median of 4 (min 0-max 8) additional serious complaints (with an ESAS score of >5). The most common interventions included intravenous hydration, analgesic and/or antiemetic administration (n=66); nutritional support (n=62), and pain specialist consultations (n=59). Thirty-three patients (19%) were referred to the inpatient or intensive care unit for emergency hospitalization. Total mortality within the 30 days following the first visit to the integrated palliative care outpatient clinic was 17%.

Conclusion: Our initial experience with the integrated palliative care clinic included patients in the advanced stages of the disease, patients with multiple serious symptoms, and patients with high mortality risk. The management of these patients in an oncology clinic-integrated setting can meet their palliative care needs, allow providing treatment interventions timely, reduce the number of unnecessary diagnostic tests and emergency department admissions.

Keywords: Edmonton, integrated clinic, palliative care

Median Age (minimum-maximum)	60.5 (17-91)
Male/Female	94 (58%) / 80 (42%)
	Stage 1: 4 (2.5%)
Discours Street (1/2/2/4)	Stage 2: 7 (4.5%)
Disease Stage (1/2/3/4)	Stage 3: 18 (11.5%)
	Stage 4: 128 (81.5%)
	ECOG 0: 19 (10.9%)
	ECOG 1: 50 (28.7%)
ECOG Performance Score (0/1/2/3/4)	ECOG 2: 36 (20.7%)
. ,	ECOG 3: 40 (23%)
	ECOG 4: 25 (14.4%)
	Gastrointestinal: 53 (30.5%)
	Lung: 43 (24.7%)
	Genitourinary: 15 (8.6%)
Tumor Location	Breast: 14 (8%)
	Gynecological: 11 (6.3%)
	Head and neck: 9 (5.2%)
	Other: 29 (16.7%).)

Table 1. Main characteristics of the patients



The Effect of Lycopene on Human Cervical Cancer Cells

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Introduction: Cervical cancer is the third most common gynecological tumor leading to death in the USA. Lycopene is a carotenoid found in many plants and it is a pigment, giving these plants their red color. Despite the establishment of anti-cancer efficacy of lycopene in many types of tumors, its effects on cervical cancer are not fully known. The aim of this study has been to determine whether lycopene alone will show effects on human cervical cancer (HeLa) cells and how and via which mechanism it will affect the actions of cisplatin, which is one of the most commonly used chemotherapeutic drugs in cervical cancer.

Materials-Methods: Hela cells were exposed to lycopene (10 uM) or cisplatin (1 uM) alone or in combination. After 72 hours, cell viability was determined by the MTS test. The expression levels of various regulatory proteins in the cells exposed to these agents were evaluated by the Western blot test.

Result: A 72-hour treatment of HeLa cervical carcinoma cells with lycopene (10 uM) or cisplatin (1 uM) or the combination of both was investigated for their effects on cell viability. It was observed that cell viability was reduced by 28.9%, 34.4%, and 62.6% after the treatment with lycopene 10 uM, cisplatin 1 uM, and the combination of lycopene and cisplatin, respectively (p<0.05). The expression levels of apoptosis-related proteins, namely Bcl-2, Bax, NF-κB, Nrf2 were examined to demonstrate the mechanism of action of lycopene. The combination of lycopene and cisplatin resulted in increased levels of apoptosis-inducing Bax and Nrf2 proteins and decreased levels of apoptosis-inhibiting Bcl-2 and NF-κB proteins compared to cisplatin administration alone (p<0.05, Fig. 1).

Conclusion: Lycopene, found in many plants, is more than a color pigment, affecting several types of tumors. Our study showed that lycopene increased the sensitivity of human cervical cells to cisplatin as observed in reduced cell viability and induction of apoptosis.

Keywords: Apoptosis, cervix cancer, lycopene

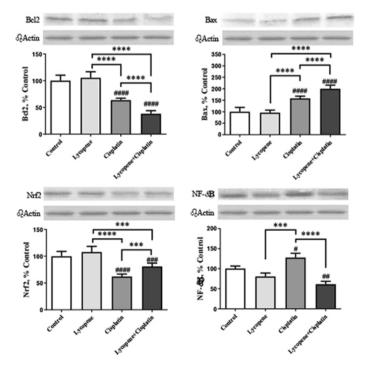


Figure 1. Effects of lycopene on apoptosis-related proteins



Malignant Melanoma: Clinicopathological Features and Prognostic Significance of Neutrophil-Lymphocyte Ratio

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Introduction: Malignant melanoma (MM) is a neoplasm characterized by high rates of metastasis and mortality. The aim of this study was to investigate the relationship of neutrophil-lymphocyte ratio (NLR) on prognosis and survival in MM, along with demographic and clinicopathological parameters.

Patients/Methods: A total of 107 patients; who were followed up in the Department of Medical Oncology, Faculty of Medicine, Eskişehir Osmangazi University in the period from the year 2010 to 2017 were evaluated retrospectively. The age and sex distribution of the patients; the levels of LDH, the neutrophil and lymphocyte counts, pathological parameters, and BRAF mutation status were examined along with their correlations with each other and the effects of these parameters on overall survival (OS) and disease-free survival (DFS) were investigated.

Results: Of the study patients; 86% were in the early stage and 14% were in the metastatic stage. Of the patients in Stage III; 65.2% (n: 23/107) had received adjuvant interferon treatment. Cutaneous involvement was common and the nodular MM were the predominant type. The most common sites of metastasis were respectively the lungs (64.7%), distant lymph nodes (40.4%), and the liver (39.2%). Of the 39 patients, for whom BRAF mutation status was investigated; BRAF V600 was positive in 53.8%. Median NLR was 1.97. All non-cutaneous MM cases were negative for BRAF (p<0.0001). No correlations were found between the presence of BRAF mutations and the following parameters including the levels of NLR and serum LDH, lymph node (LN) involvement, the disease stages, the pathologic parameters, and the distribution of age and sex. In the advanced disease stages, the incidences of high NLR and non-cutaneous MM were higher (p=0.001). A high NLR was found out to be correlated with advanced age (p=0.008), tumor ulceration (p=0.011), and the high mitosis rates in the tumor (p=0.05). Median OS was 13, 45, 84, 101 months for the advanced stage, stage III, stage II, and stage 0-I, respectively. A high NLR (p<0.0001), LDH levels (p=0.04), increased Breslow thickness (p=0.01), Clark levels (p=0.01), the number of mitosis (p=0.02), presence of ulcerations (p=0.03), and LN involvement (p=0.04) were significantly associated with a shorter OS duration. Median DFS was 40 months in stage II and 23 months in stage III. DFS was significantly shorter in patients with increased Breslow thickness (p=0.01), high Clark levels (p=0.05), a high number of mitosis (p=0.02), and LN involvement (p=0.03). Cox regression analysis revealed that the most significant parameters affecting OS were NLR (HR: 3.4, p=0.04) and the presence of a nodal disease (HR: 4.6, p=0.01). Nodal involvement was additionally found out to be the most significant predictor of recurrences (HR: 3.2, p=0.03).

Conclusion: NLR appears to be an additional biomarker to the classical ones for predicting prognosis. Patients with nodal involvement and high NLR should be closely monitored in the clinical practice. There is a need to prove the data, conducting large-scale studies.

Keywords: Clinicopathologic features, malignant melanoma, NLR

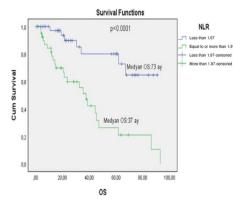


Figure 1. Change in the overall survival length in association with the neutrophil-lymphocyte ratio (Kaplan Meier analysis).

Table 1. Independent variables predictingdeath in the Cox multivariate analysis

Independent Variables	HR (Hazard Ratio)	p-value
Lymph node involvement	4.6 (1.2-16.8)	0.01
NLR	3.4 (1-11.9)	0.04
LDH	2 (0.5-7.9)	0.2
Breslow thickness	2.2 (0.6-8.2)	0.2
Gender	0.4 (0.08-2.9)	0.4
Number of Mitosis	0.3 (0.03-5.1)	0.4
Presence of ulcerations	0.4 (0.03-4.9)	0.4

Table 2. Independent variables predicting death in the Cox multivariate analysis

Independent Variables	HR (Hazard Ratio)	p-value
Lymph node involvement	3.2(1-10)	0.03
Number of Mitosis	2.3 (0.7-7.5)	0.1
Breslow thickness	1.9 (0.6-5.9)	0.2
LDH	0.4 (0.1-1.5)	0.2
NLR	1.6 (0.4-6.1)	0.4
Presence of ulcerations	0.9 (0.1-4.1)	0.8



Adenoid Cystic Carcinoma: Experience of Two Centers

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Adenoid cystic carcinoma is a rare malignant tumor, originating mainly from the major and minor salivary glands. It is rarely seen in the tracheobronchial tree, breasts, skin, the female genital system, and the prostate. While surgery and radiotherapy are effective to control the tumor locally, effective treatment options for the metastatic disease are still investigated. Because of long survival and late metastasis, identification of the factors affecting the survival have gained importance.

In this study, we aimed to present the survival data and find out prognostic markers in patients with adenoid cystic carcinoma.

Patient data from two centers were included in the study. Patients receiving the diagnosis of adenoid cystic carcinoma in the period from 1998 to 2018 were reviewed retrospectively. Of these patients; 14 (53.8%) were women and 12 (46.2%) were men, with a median age of 51 (32-70) years at the time of the diagnosis. At the time of the diagnosis, 5 patients were at stage 1 (19%), 7 were stage 2 (26%), 7 were stage 3 (26%), and 7 were stage 4 (26%). Of these patients, 3 (11%) had distant organ metastases. Twenty-three patients underwent curative surgery. Of them, 8 underwent R0 resection and 15 underwent R1 resection. Local recurrences were found in 46% of the patients and the most common site of metastasis was the lungs (38%).

The median length of follow-up was 97 (63.9-129.8) months. At the time of analysis, 23 of 26 patients had progressed (89%) and 11 (57.7%) had died. One-year survival rate was 100%, 2-year survival rate was 96.3%, three-year survival rate was 83%, and 5-year survival rate was 78%. No differences were found out in the survival rates based on sex or smoking status. The median length of overall survival was 124 months (95% CI 72.6-175.8). The median overall survival was found to be 124 months in the tumors with non-salivary gland location and it was 84 months in the tumors located in the salivary glands. The difference between these figures did not reach a statistical significance (p=0.22). While the median survival was 124 months in the group undergoing surgery, it was found out to be 28 months in the non-surgically treated group. The numerical difference between these figures was not statistically significant (p=0.071). Although R0 resection numerically contributed to the survival coefficient compared to R1 resection (198 months, 102 months respectively); this numerical difference did not reach statistical significance (p=0.18).

In our study, numerical differences between the figures were not statistically significant because of the small number of patients. We suggest that surgical intervention, R0 resection, and a non-salivary gland location of the tumor will be found out to be good prognostic factors if the study is carried out by including a larger patient group.

Keywords: Adenoid cystic carcinoma, prognostic factors, survival

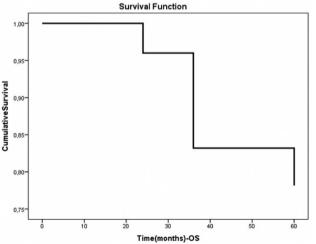


Table 1. Prognostic factors

	Survival (months)	p-value
Patients, who underwent surgery	124.3	0.071
Patients who did not undergo surgery	28.4	
R0 resection	198.7	0.188
R1 resection	102.8	
Location other than the salivary glands	124.3	0.22
Located in the salivary glands	83.9	

Figure 1. Overall Survival



Clinical and Pathological Features of HER2 Positive Gastric Cancer Patients: A Single Center Experience

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Objective: The proven clinical efficacy of trastuzumab in HER2-positive gastric cancer patients paved the way for these patients to be evaluated as a different subgroup. The aim of this study was to evaluate the demographic and pathological features of HER2 positive gastric cancer patients.

Materials-Methods: The data of 14 patients; who were treated and followed up in the period from 2017 to 2018 in the medical oncology clinic of Antalya Training and Research Hospital, were collected retrospectively. The relationship of HER2 positivity with the following parameters; including age, tumor location, histopathological subtype, and the presence of lymphovascular and perineural invasion was evaluated. The Chi-square test was used for the statistical analysis.

Result: The mean age was 55 (31-70) years. All HER2 positive patients were males and their ECOG performance status was found out to be 0. Tumor location of HER2 positive patients were as follows: The tumor location in the stomach was in the cardia in 2 (14%) patients, in the fundus in 4 (29%) patients, and in the corpus in 8 (57%) patients. The histopathological examinations demonstrated that signet ring cell carcinoma was present in 6 (43%) patients and adenocarcinoma in 8 (53%) patients. Diffuse type was found in 4 (29%) patients and intestinal type gastric cancer was detected in 10 (71%) patients. In HER2 positive patients; lymphovascular invasion was seen in 12 patients (86%) and perineural invasion was observed in 86% of the patients.

Conclusion: In this study, we shared the clinical and pathological features of HER2 positive patients. However, the number of cases and the length of follow-up period are limited. Multi-center studies to be carried out with long-term follow-up periods are necessary to collect and share data to precisely define the histopathological features of HER2 positive patients and to determine the efficacy of trastuzumab in our country.

Keywords: HER2, pathological features, stomach cancer



Prognostic Significance of Systemic Inflammatory Index (SII) in Metastatic Renal Cell Carcinoma (mRCC)

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Objective: To investigate the prognostic significance of systemic inflammatory index in patients with metastatic renal cell carcinoma.

Methods: The data from 53 metastatic RCC patients admitted to the Medical Oncology Department of our hospital were analyzed retrospectively. The patient data; including the complete blood count parameters at the time of diagnosis, treatments received, the length of treatment, treatment responses, the date of the last control visit, and the survival status were documented. Systemic inflammatory index was calculated using the following formula: neutrophil count X lymphocyte count)/ platelet count. The results were analyzed with the Receiver Operating Characteristic (ROC) test. The patients were divided into high-risk and low-risk groups according to the calculated cut-off values. Then, the survival data of these groups were compared with the Kaplan-Meier analysis. A p-value of <0.05 was considered significant.

Result: Data from 31 patients were analyzed in our study. The median age of the patients was 62 years (range: 28-84 years), the number of male patients was 25 (80.6%), and the number of female patients was 6 (19.4%). The median tumor size in the whole group was 8 cm (range: 2-18 cm). The histological features of the tumors were mostly indicative of the clear cell sub-type (n: 29, 93.5%). The median follow-up period was 25.3 months (range: 3.0-108.0 months). The median survival was 46.0 months (95% Cl: 1.17-90.8) in the whole study group. Taking the survival as the primary endpoint in the ROC analysis, the area under curve (AUC) was calculated as 0.783 (95% Cl; 0.614-0.953) with a p-value of =0.007 and the optimal cut-off value was found as 10.02×10^5 . The low and high-risk patients were defined as the patients with a SII score of $\leq 010.02 \times 10^5$ and a SII score of $>10.02 \times 10^5$, respectively. There were no statistically significant differences in the main clinical and pathological features between the two groups (Table 1). When the lengths of survival were compared between these two groups, a statistically significant difference was obtained. While the median length of survival was not found in the low-risk group, the median survival in the high-risk group was found out to be 21.9 months (95% Cl; 9.7-34.1) (p<0.001) (Fig. 1).

Conclusion: Systemic inflammatory index; which has been investigated in many solid tumors and which was proved to have a prognostic significance, can be a useful prognostic parameter in metastatic RCC patients. The major limitation of our study was its retrospective nature and the small number of study patients.

Keywords: Metastatic renal cell carcinoma, prognosis, systemic inflammatory index

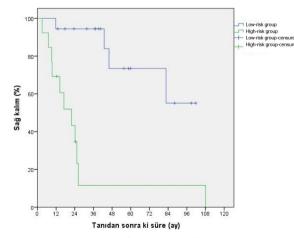


 Table 1. Key characteristics of low-risk and high-risk patients

	Low-risk patients (n: 18)	High-risk patients (n: 13)	p-value
Age	62.5 (28-79)	62.0 (45-84)	0.737
Sex Male Female	14 (77.8%) 4 (22.2%)	11 (84.6%) 2 (15.4%)	0.501
Tumor Size	8.7 (2-189)	7.0 (3.6-14.5)	0.323
ECOG score 0-1 2 or higher	17 (94.49%) 1 (5.6%)	11 (84.6%) 2 (15.4%)	0.376

Figure 1. Survival curves for low-risk and high-risk patients



Relationship Between Prognostic Nutritional Index (PNI) and Survival in Patients with Metastatic Renal Cell Carcinoma

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Introduction: The significance of prognostic nutritional index (PNI) has been shown in several cancer types. In this study, we aimed to determine the prognostic significance of PNI in patients with metastatic renal cell carcinoma (RCC).

Methods: The data from 51 metastatic RCC patients admitted to the Medical Oncology Department of our hospital were analyzed retrospectively. Complete blood count, metabolic parameters, treatments received, length of treatment, responses to treatment, the date of the last control visit, and the survival status of the patients were documented. Prognostic nutritional index was calculated with the following formula: 10 X albumin (g/dl) + (0.005x lymphocyte count). A p-value of <0.05 was considered significant.

Results: The data from 51 patients were analyzed in our study. The median age of the patients was 60 years (range: 28-84); the number of male patients was 38 (74.5%), and the number of female patients was 13 (25.5%). The median tumor size in the whole study group was 7.5 cm (range: 1.8-18 cm) and tumor histology was mostly indicative of the clear cell subtype (n: 42, 82.4%). The median follow-up period was 25.3 months (range: 3.0-108.0 months). Median survival in the whole group was 46.0 months (95% CI; 18.9-73.1). In the univariate analysis performed with Cox regression, survival was the endpoint; however, prognostic nutritional index did not have a statistically significant association with survival. According to the obtained results, Hazard Ratio (HR) was found out to be 0.97 (% GA; 0.83-1.13) p=0.747.

Conclusion: Prognostic nutritional index has been investigated for its prognostic significance in many solid tumors and has been found out to be significantly associated with some types of tumors. However, PNI was not associated with survival in metastatic RCC patients in this study. The major limitation of our study was its retrospective nature and the small number of study patients.

Keywords: Pni, prognosis, renal cell cancer



Clinical Significance of PRAME and PDL-1 Expression in Colon Cancer

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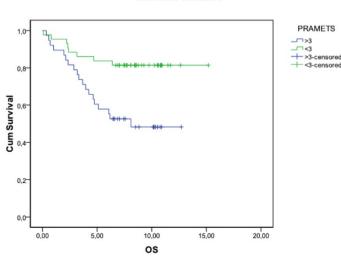
Objective: PRAME (Preferentially expressed antigen of melanoma) belongs to the family of cancer testicular antigens and it is highly expressed in various solid tumors and in the normal testicular tissue. PRAME was first isolated as a human melanoma antigen recognized by cytotoxic T-lymphocytes. Besides hematopoietic cells, PD-L1 is expressed on the surface of most tissue types, including many tumor cells, and interacts with PD1 to inhibit apoptosis in tumor cells. In this study, the clinical significance of PRAME and PDL-1 expression was investigated in patients with colorectal cancer receiving adjuvant therapy.

Methods: The study included 81 patients receiving adjuvant chemotherapy for the treatment of stage II and stage III colon cancer in the School of Medicine Hospital of Çukurova University. Age, sex, the date of diagnosis, the date of progression, the date of death if relevant, tumor size, lymph node metastasis, tumor location, tumor differentiation, additional component types in the tumor, and the LVI and PNI status were retrieved from the hospital information system. The disease stages of the patients were defined according to the TNM staging system. Immunohistochemical kits for PRAME and PDL-1 expression were used in the tests.

Result: Of the study patients; 48% were females and the mean age of the patients was 56 years. The right colon was involved in 49% of the patients. In 51% of the patients, the left colon was involved. Of all study patients, 33% died in the 5-year followup period. The tumor size and the number of metastatic lymph nodes were not statistically significantly associated with the following variables including the PRAME density, PRAME proportion scores, and the PRAME total scores of >3 (p>0.05). PRAME was found to affect survival; however, PDL-1 levels had no effects on survival. It has been found that the PRAME density scores, which determine the PRAME gene expression, was better in determining progression-free survival (PFS) compared to the PRAME proportion score (p=0.046 vs p=0.071, respectively). It was found that the PRAME total scores of >3 was statistically significant in determining PFS (p=0.024) and OS (p=0.004).

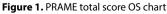
Conclusion: Because the PRAME total scores of >3 are associated with short PFS and OS, these patients should be followed up more actively compared to the patients with PRAME total scores of <3 to detect disease progression earlier.

Keywords: Colon cancer, PRAME, PDL-1



Survival Functions

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The Relationship of the Newly Introduced Inflammatory Prognostic Index with Survival in Metastatic Esophageal Squamous Cell Carcinoma

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Introduction: Esophageal squamous cell carcinoma (ESCC) is one of the most aggressive tumor types in the world and malnutrition is common in these patients. Inflammation and nutrition play critical roles in the disease prognosis. The aim of this study was to investigate the relationship of the newly introduced inflammatory prognostic index (IPI) with C-reactive protein (CRP), albumin, and the neutrophil and lymphocyte counts at the time of diagnosis in patients with metastatic ESCC.

Materials and Methods: Patients who were admitted to Van Yüzüncü Yıl University's Medical Oncology Clinic due to a metastatic ESCC at the time of diagnosis and who had not previously received chemotherapy were included in the study. Patients were excluded if they were younger than 18 years old, had a stage 4 disease, and had no squamous pathology. The IPI score was calculated with the following formula: CRP X NLR (neutrophil/lymphocyte ratio) / Albumin. The cut-off value of the IPI score for overall survival was calculated by plotting the ROC curve. The IPI index was found to be 4.0 with 75% sensitivity and 93% specificity. The patients were divided into two groups according to their IPI scores as patients with scores of <4 in one group and patients with scores of \geq 4 in the other group.

Result: A total of 34 patients, 15 (44.1%) males and 19 (55.9%) females, were included in the study. The number of patients with IPI scores of <4 was 12 (35%) and the number of patients with IPI scores of \geq 4 was 22 (65%). The median age was 67 (49-78) in the IPI <4 group and 61 (43-85) in the IPI \geq 4 group. The demographic characteristics of the patients and the intergroup comparisons are shown in Table 1. Overall survival was 16 months (13.3-18.2) in the IPI <4 group and 5 months (3.2-6.7) in the IPI \geq 4 group (Log-rank p=0.002) (Fig. 1).

Conclusion: In our study, the IPI score was found to be significantly associated with survival in patients with metastatic ESCC. It was found out that $IPI \ge 4$ was significantly associated with reduced overall survival. In conclusion, IPI score may be an inexpensive, easily accessible, and independent prognostic index in patients with metastatic ESCC. However, larger scale studies are needed to confirm these findings.

Keywords: Esophageal squamous cell carcinoma, inflammatory prognostic index, survival, prognosis

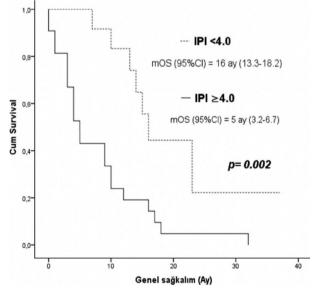


Figure 1. Overall survival curves according to low and high IPI scores.

 Table 1. Inter-group relationships according to the demographic characteristics and the IPI scores of the patients

		All patients		IPI <4.0		$\rm IPI \geq 4.0$		p.
		n	%	n	%	n	%	
Gender	Male	15	44.1	4	33.3	11	50	0.350
	Female	19	55.9	8	66.7	11	50	
ECOG PS	0	2	5.9	2	16.7	0	0	0.135
	1	24	70.6	9	75	15	68.2	
	2	4	11.8	1	8.3	3	13.6	
	3	4	11.8	0	0	3	18.2	
Localization	Upper	3	8.8	0	0	3	13.6	0.123
	Middle	18	52.9	9	75	9	40.9	
	Lower	13	38.2	3	25	10	45.5	
First series of chemotherapy	No	1	3.7	0	0	1	6.7	0.272
	Yes	26	96.3	12	100	14	93.3	
Final outcome	Death	28	82.4	7	58.3	21	95.5	0.007
	Right	6	17.6	5	41.7	1	4.5	



Prognostic Factors in Breast Cancer Patients

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Objective: Breast cancer is the most common type of cancer in women. One in eight women has a risk of developing breast cancer. The aim of this study was to evaluate the relationship between prognostic factors and survival in breast cancer patients.

Material-Method: SPSS (version 21; IBM, Armonk, NY) package program was used for investigating the correlation of the demographic and clinical characteristics with survival. Kaplan-Meier method was used for plotting the survival curves and logrank test was used for carrying out survival analysis associated with the prognostic factors.

Results and Conclusion: The median overall survival was 72 months (95% CI 45.29-98.70) in a total of 103 breast cancer patients included in the statistical analysis. In our study; young age, smoking, family history of cancer, and histological grading were found out to affect survival. This study has evaluated the characteristics of survival characteristics and related factors affecting survival in the patients, who were followed up for breast cancer.

Keywords: Breast cancer, prognostic factors, survival analysis



Factors Affecting Survival Outcomes in Breast Cancer Patients Younger than 40 Years Old

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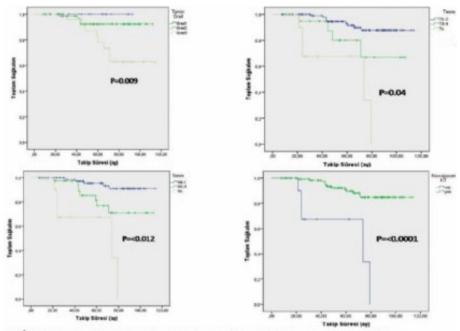
Objective: Breast cancer remains to be a major health problem worldwide. The increase in the incidence of the disease and the rise in cancer-related mortality rates in women younger than 40 years old suggest that this problem will continue. It is known that the disease has a more heterogeneous, more aggressive and complex biology in young patients. The aim of this study was to determine the prognostic factors affecting the survival of \leq 40 years old patients admitted to our hospital for treatment.

Materials-Methods: This is a retrospective study. The patients; who were ≤40 years old at the time of diagnosis and who had received curative RT for the treatment of a non-metastatic unilateral invasive breast cancer were included in the study. The following parameters were examined in the study; including the tumor histopathology, treatments administered, and other prognostic parameters.

Result: A total of 146 patients were included. Patient characteristics are summarized in Table 1. The mean overall survival (OS) was 101 (96-106) months. OS at the year 2, 5, and 7 were 97%, 88%, and 80%, respectively. The univariate analyses revealed that tumor grade (Grade 1 vs Grade 2 vs Grade 3; p=0.009), T-stage (T1-2 vs T3-4; p=0.04), N-stage (N0-1 vs N2-3; p=0.012), and receiving neoadjuvant chemotherapy (CT) (0=<0.0001) were the statistically significantly associated factors. The multivariate analyses revealed that receiving neoadjuvant CT [p=<0.0001; HR = 20.76 (5.71-75.49)] and having an N2-3 disease [p=0.02; HR=3.79 (1.22-11.73)] were the most important factors increasing the risk of death. The mean disease-free survival (DFS) was 90 months. The DFS for 2, 5, and 7 years were 96%, 83%, and 69%, respectively. In the univariate analyses, the N stage (N0-1 vs N2-3; p=0.017) and receiving neoadjuvant CT (0=<0.0001) were found to be statistically significant. In the multivariate analyses, receiving neoadjuvant CT (p=0.001; HR=12.09 (4.65-31.43)] and having an N2-3 disease [p=0.02; HR=2.43 (1.14-5.17)] were found to be the most important factors increasing the risk of progression.

Conclusion: It is remarkable that; besides the other known conventional prognostic factors, receiving neoadjuvant CT was found to be the most important prognostic factor unfavorably affecting the survival of patients under 40 years of age. The study needs to be supported with the results of studies conducted on larger patient series.

Keywords: Breast cancer, survival, young



ŞEKİL 1a-d: Tek değişkenli analizlerde toplam sağkalıma etki eden prognostik faktörler Figure 1.

	Table	1. Patient	characteristics
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Variables		n=146	%
Age		36 (27-40)	
Surgery	Modified Radical Mastectomy	95	6
	Breast-conserving Surgery	51	35
Tumor Grade	Grade 1	20	14
	Grade 2	81	55
	Grade 3	29	20
	Unknown	16	11
Tumor stage	nTJ-2	112	73
	pT3-4	21	14
	Neoadjuvant CT	13	9
Nodal stage	pN0-1	90	62
	pN2-3	43	25
	Neoadjuvant CT	13	9
Hormonal status	ER (+) PR (+) HER2 (-)	72	49
	ER (+) PR (+) HER2 (+)	42	30
	ER (-) PR (-) HER2 (+)	15	10
	Triple (-)	17	11
ECE	Yes	78	53
	No	45	31
	Unknown	23	16
LVI	Yes	60	41
	No	52	30
	Unknown	34	23
CT status	Neoadjuvant CT	13	9
	Adjuvant CT	126	80
	No	7	5
RT-treated regions	GD	45	31
	GD+Supra	96	60
	GD+Supra+MI	5	3



Correlation of PET-CT and Bone Marrow Biopsy Results to Evaluate Bone Marrow Infiltration in HL Case Series

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Introduction: Hodgkin lymphoma (HL) accounts for 10% of all lymphomas. It is categorized under two headings as classical and nodular lymphocyte-predominant HL (NLPHL). The classical type is further subdivided into the nodular sclerosing (NS), mixed cellular (MC), lymphocyte-rich (LR) and lymphocyte-poor (LP) subtypes (1). The incidence of bone marrow infiltration (BMI) in HL is 4-18%. The results of bone marrow biopsy (BMB) is used for disease staging (2). Because BMB is invasive and painful, PET-CT has recently been introduced as another major tool to optimize staging (3). The aim of our study was to compare BMB and PET-CT to evaluate BMI.

Material-Method: A total of 110 patients admitted to our clinic due to the diagnosis of HL were evaluated retrospectively. The patients were included if they had undergone both BMB and PET-CT for staging. BMB was considered the standard method for staging. The findings from BMB were correlated with those of PET-CT imaging.

Results: Of the 110 patients, 70 (64%) were males and 40 (36%) were females. The mean age of the patients was 37.45 (18-79) years. NC subtype was found in 83 (75.45%) patients, MC in 17 (15.45%), NLP type in 7 (6.36%), LP in 2 (1.82%), and LR was identified in 1 (0.91%) patient. The disease stages were as follows: Seven patients (6.36%) had stage 1 disease, 28 patients (25.45%) had stage 2 disease, 52 patients (47.27%) had stage 3 disease, and 23 patients (20.91%) had stage 4 disease. Out of 110 patients, BMI was positive in 13 (11.81%) and negative in 97 based on the BMB results. PET-CT imaging showed the presence of BMI in 44 patients (44.54%) and reported negative results in 61 patients. In 11 BMI-positive patients and 59 BMI-negative patients, the findings of BMB and PET-CT results were correlated. The PET-CT imaging reported 38 patients as BMI-positive; who were in fact BMI-negative based on the BMB results. PET-CT imaging results were BMI-negative for 2 patients; who were in fact BMI-positive based on the BMB biopsy results. BMI positivity or negativity were correlated in the BMB and PET-CT imaging results of 64% (n: 70) patients; whereas, their results were not correlated in 36% (n: 40) patients. Based on the consideration that BMB is the gold standard in detecting BMI; the sensitivity and specificity of PET-CT imaging was found out to be 84% and 60%, and the positive and negative predictive values were 22.4% and 96.7%, respectively.

Discussion-Conclusion: Staging is a crucial step to determine the treatment strategy in HL. BMB is the gold standard method for detecting BMI; however, it is an invasive and painful procedure. In recent years, BMB has been replaced by PET-CT. In our study, 11 (10%) patients were diagnosed with BMI by BMB. BMI was diagnosed in all of these patients by PET-CT, too. PET-CT results were false positive in 38 (34.5%) patients, diagnosing these patients with BMI but they were actually BMI-negative as confirmed by BMB. PET-CT results were false negative in 2 patients (1.8%); who were actually BMI-positive as evidenced by BMB. BMB and PET-CT are complementary tests to identify BMI in HL. BMB results remain to be important parameters for staging.

Keywords: Bone marrow biopsy, bone marrow infiltration, hodgkin lymphoma, PET-CT



The Role of Tyrosine Kinase Inhibitors in the Treatment of Advanced Medullary Thyroid Cancer

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Objective: Medullary thyroid cancers (MTC) are rare neuroendocrine tumors. They account for 1-2% of all thyroid cancers. The only known curative treatment of MTC is surgery. Chemotherapy, immunotherapy, and treatment with tyrosine kinase inhibitors (TKIs) improve the progression-free survival (PFS) in the locally advanced or metastatic inoperable disease. In this report, we aimed to present the data of patients who were followed up and received treatment with TKI in our clinic.

Methods: Patients who were followed up at Okmeydani Training and Research Hospital's Medical Oncology Clinic and who received TKI for advanced stage MTC were included in the study. Disease progression was determined based on the PET Response Criteria in Solid Tumors (PERCIST) on Ga-68 DOTA-TATE PET/CT imaging. The patients without Ga-68 DOTA-TATE PET/CT imaging were not included in the study.

Results: A total of 8 patients were included in this retrospective study. Of them, 3 (37.5%) were male and 5 (62.5%) were female. The mean age of the patients was 54.2 years. All patients had the sporadic form of MTC and the disease stage was IVC in all patients. All patients had cervical and lower mediastinal lymph node metastases. Bone metastases, lung metastases, and liver metastases were present in 4 (50%), 3 (37.5%), and in 2 (25%) patients, respectively. One (12.5%) patient received cabozantinib treatment and 7 (87.5%) patients were treated with vandetanib. The median length of the follow-up period was 17.8 months; during which a median PFS could not be achieved. Partial response was obtained in 3 (37.5%) patients; 4 (50%) patients were stable, and the treatment was discontinued in 1 (12.5%) patient due to torsades de pointes associated with a long QT syndrome.

Conclusion: Both vandetanib and cabozantinib improve progression-free survival in patients with locally advanced or metastatic inoperable MTC. With this presentation, we have emphasized the importance of TKI therapy in patients with MTC, which we rarely encounter in clinical practice.

Keywords: Medullary thyroid cancer, tyrosine kinase inhibitor, vandetanib



Prognostic Significance of Albumin to Globulin Ratio in Patients with ALK Mutation

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Introduction: Inflammation is associated with poor prognosis in many types of cancer, besides facilitating cancer development. Although albumin and globulin are the markers indicating the presence of inflammation, they may be affected by many non-inflammatory factors. Therefore, it is suggested that albumin to globulin ratio (AGR) will predict inflammation more successfully. In this study, we aimed to investigate the prognostic significance of albumin-to- globulin ratio (AGR) in patients with an ALK mutation.

Methods: The patients; who were diagnosed in the period from 2014 to 2018, who had an ALK mutation, who had a metastatic disease, and who received crizotinib regardless of the treatment line were included in the study to be evaluated retrospectively. AGR at the time of the diagnosis was found by dividing the level of albumin by the level of globulin. Accepting the cut-off value as 1.2, the patients were divided into two groups as the patients with AGR values of \geq 1.2 and <1.2.

Results: Fifty-one patients with metastatic lung cancer positive for ALK mutations were included in the study. Of the patients, 62.7% had AGR values of \geq 1.2 and 37.3% had AGR values of <1.2. The comparison of the baseline demographic and clinical characteristics of the patients revealed no significant intergroup differences in the evaluated parameters, excluding the CRP levels. Detailed information is presented in Table 1. After a median follow-up period of 16.8 months, progression-free survival (PFS) with crizotinib was significantly better in the AGR \geq 1.2 group. The median PFS was found to be 24 months in the AGR \geq 1.2 group and 7 months in the <1.2 group (p<0.001) (Fig. 1). The median overall survival (OS) was found to be 36.9 months in AGR \geq 1.2 group, and 10.6 months in the AGR <1.2 group (p=0.009).

Conclusion: AGR can be used as a prognostic marker in ALK positive lung cancer because it is both easy to perform and inexpensive. To the best of our knowledge, this is the first study to investigate the prognostic efficacy of AGR in patients with the ALK mutation.

Keywords: Albumin, ALK, globulin, lung

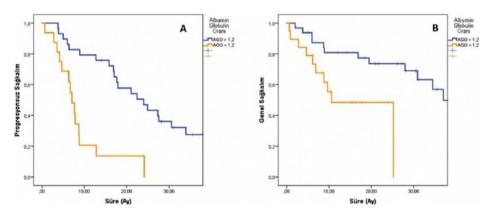


Figure 1. Prognostic effect of albumin to globulin ratio (AGR) on progression-free and overall survival

Table 1. Demographic Characteristics ofthe Patients

PARAMETER	AGR <1.2	$AGR \ge 1.2$	p.
Age (Median, min-max)	51.5 (26-82)	49.5 (27 - 70)	0.96
Sex (%) Male Female	55.6 44.4	53.1 46.9	0.709
Smoking Status (%) Never smoked Stopped smoking Smoker	66.7 26.7 6.6	69.2 26.9 3.8	0.906
BMI (kg/m2, Median)	26	25.7	0.93
Crizotinib Step (%) Step 1 Step ≥ 2	50 22.2 27.8	46.9 40.6 12.5	0.313
Brain Met (%) Yes No	31.3 68.8	34.5 65.5	0.58
Liver Met (%) Yes No	27.8 72.7	26.5 73.5	0,64
Adrenal Met (%) Yes No	33.3 66.7	12.5 87.5	0.057
Counter Lung Met (%) Yes No	38.9 61.1	43.8 56.2	0.23
Pleural Met (%) Yes No	38.9 61.1	34.4 65.6	0.901
CRP (mg/dL)	5.3	1.77	0.04
LDH (mg/dL)	219	231	0,73
Neutrophil (K/l)	5545	4100	0.097
Lymphocyte (K/l)	1400	1890	0.157

AGR - Albumin to globulin ratio, BMI - Body mass index, Met - Metastasis



Distribution of Mutation Outcomes According to Stages and Localization in Metastatic Colon Cancer

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Objective: To evaluate the distribution of mutation outcomes according to the disease stages and tumor localization in patients with metastatic colorectal cancer treated in our center.

Method: Clinicopathologic features of 38 patients with metastatic colon cancer were evaluated. Surgical treatment of the primary tumor, the metastasectomy status, tumor location, and mutation analyses were recorded in the patients.

Results: At the time of the diagnosis; 28 patients had "de novo" metastases and 10 had either stage 2 or 3 disease. Twelve patients had undergone surgery for primary colon cancer. Eight patients had undergone metastasectomy. Of the patients; 47% were PanRAS wild, 3% were BRAF positive, and 50% had KRAS and Nras mutations. The most common type of mutation was KRAS on exon 2. The second most common type of mutation was mutation was NRAS on exon 3. PanRAS wild was diagnosed in the early disease stage in 7 out of 18 patients. 85% of RAS mutant patients were diagnosed in the metastatic period. The left colon was involved in 29 patients and the right colon was involved in 9 patients. PanRas Wild was detected in 22% of the right colon patients and 58% of the left colon patients were of the wild type.

Conclusion: Mutation rates were higher in the patients with denovo metastatic disease at the time of diagnosis and in the right-sided colon cancer patients. In the literature, Ras mutation rates in the right-sided colon cancer were found to be higher compared to the left-sided colon cancer. Kras mutation was not found to be associated with prognosis in the right-sided colon cancer but was associated with poor prognosis in the left-sided colon cancer.

Keywords: Metastatic colon cancer, RAS mutation analysis, tumor location



Comparison of the 12-Month Trastuzumab Therapy with a Shorter Treatment Regimen as Adjuvant Treatments for Her2-Positive Breast Cancer

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Introduction: In this study, we aimed to compare the survival data of patients who received trastuzumab for less than 12 months (short treatment) for any reason with the survival data of the patients who received trastuzumab for 12 months (standard treatment).

Material-Method: The patients; who were admitted to our outpatient clinic for HER2 positive breast cancer at stage 2-3 in the period from 2011 to 2018, were evaluated retrospectively. A total of 136 patients were included in the study. Of these patients, 85 received standard-duration trastuzumab therapy and 51 received short term trastuzumab treatment.

Results: The median age of the patients was 50 years (range: 19-80 years). Fifty percent of the patients were pre-menopausal and 73% had positive hormone receptors. Of all patients; 53% were at stage 3. The median duration of trastuzumab use in the short-term treatment group was 6 months (9 weeks-45 weeks). Hormone receptor positivity was lower in the standard trastuzumab therapy group but the number of patients having positive lymph nodes and the number of patients at the stage 3 were larger. There were no intergroup differences in the other types of patient characteristics. The median length of follow-up period in our study was 62.6 months. There were no intergroup differences in the 5-year disease-free survival (DFS) rates and overall survival (OS) rates (91% and 86% for DFS, respectively: p=0.1. 94% and 92% for OS, respectively: p=0.4). In stage 3 patients, DFS was better in the standard treatment group and OS was similar between the groups (92% vs 82% for DFS; p=0.05. 92% vs 89% for OS; p=0.6). In stage 2 patients, there were no intergroup differences in DFS and OS (92% vs 100% for DFS, p=0.2; 96% vs 100% for OS, p=0.4). Although cardiotoxicity occurred numerically at a higher rate in the standard treatment group, the difference was not statistically significant (9% and 4%, respectively, p=0.3).

Conclusion: There were no differences in the 5-year DFS and OS when the standard trastuzumab treatment for 12 months was compared to the shorter time of trastuzumab use. However, the disease-free survival rate in stage 3 disease was better in the patients who received trastzumab for 12 months. Adjuvant trastuzumab therapy is given to the patients to be used for one year in routine oncology practice. Some studies have shown efficacy of this treatment when used for periods of less than 12 months. However, further studies are needed to define these patients precisely so that they will be correctly selected for appropriate treatment strategies.

Keywords: Adjuvant, breast cancer, duration, trastuzumab

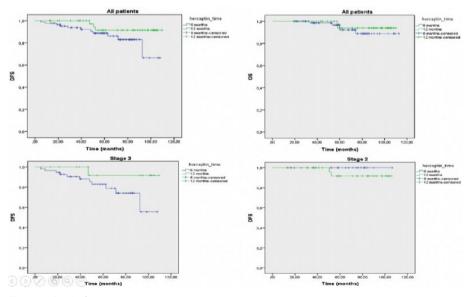


Figure 1. Survival curves



Significance of Prognostic Nutritional Index on Predicting Prognosis in Patients with Locally Advanced Lung Cancer Receiving Chemoradiotherapy

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Lung cancer is the most common type of cancer and the 5-year overall survival is still low today. Prognostic nutritional index (PNI) indicates both the nutritional and immunological status of the patient. Although PNI has been shown to correlate with prognosis in the metastatic disease, there are no studies about its prognostic value in the locally advanced disease. In our study, the association of PNI on prognosis was evaluated in stage 3 patients.

Material Method: Stage 3 patients admitted to our clinic in the period from 2012 to 2019 were included in the study. Demographic data, laboratory values, progression, and final dates of control visits about patients were documented. Patients with missing data were excluded. PNI was calculated with the following formula: serum albumin X 10 + 0.0005 X peripheral lymphocyte count (ml/mm³). PNI-values of <50 were considered to be low based on the reported PNI cut-off value of 50 in the literature. The chi-square test was used for intergroup comparisons. The association of PNI with progression free survival (PFS) was analyzed with the Kaplan-Meier method.

All of the 63 patients included in the study were males and median age was 64 years. Examination of the pathologic subtypes revealed that 7.9% of the patients had adenocancer, 69.8% had squamous cell cancer, and 22.3% had the other histological types. Thirty-three patients had low and 30 patients had high PNI values. There were no intergroup differences in age and gender distribution, disease stages or histological subtypes (Table 1). PFS was found to be 6 and 8 months respectively but the difference was not statistically different (p=0.51).

Conclusion: With the introduction of immunotherapy agents for the treatment of lung cancer, it has become important to determine the predictive and prognostic parameters that will allow for identification of the patients, who will benefit from the treatment and whose disease courses will be affected. In our study, a low PNI seems not to affect the progression-free survival in patients receiving chemoradiotherapy, but we believe that prospective larger-scale studies may yield significant results.

Keywords: Lung cancer, prognostic index, radiotherapy

PNI<50 (n:33)	PNI>50 (n:33)	p-value
66	63	0.25
33/0	30/0	NA
32 1/23/5/4	30 4/21/5/0	0.33 0.12
1/5/11/14 3/7/18/3	1/4/11/13 0/5/15/8	0.99 0.12
3/16/7/4 11.5	3/14/10/1 13.2	0.49 0.001
268,3	282.2	0.70
3.9 7.9	1.5 6.7	0.009 0.67
	66 33/0 32 1/23/5/4 1/5/11/14 3/7/18/3 3/16/7/4 11.5 268,3 3.9	66 63 33/0 30/0 32 30 1/23/5/4 4/21/5/0 1/5/11/14 1/4/11/13 3/7/18/3 0/5/15/8 3/16/7/4 3/14/10/1 11.5 13.2 268,3 282.2 3.9 1.5

Table 1. Comparison of the patients by the PNI groups



Prognostic Significance of ALBI Grades on Survival in Patients with Liver Metastasis due to Stomach Cancer

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Introduction: The baseline albumin-bilirubin (ALBI) grade was first introduced as a prognostic marker in patients with hepatocellular carcinoma. Other studies investigated ALBI grades in metastatic colorectal carcinoma and early stage stomach cancer. The aim of this study was to investigate the prognostic significance of the ALBI grades on survival in stomach cancer patients with de-novo liver metastasis.

Material-Method: The demographic and clinical data and the ALBI grades of 203 patients admitted to our clinic were retrospectively reviewed. The survival analysis by the ALBI grades were performed with the Kaplan Meier test and the univariate and multivariate analyses. Additionally, the Cox regression method was used for evaluating other factors; which might affect the survival analysis. Two different models have been developed to compare particularly the effects of albumin alone and bilirubin alone on the ALBI grades. Albumin and bilirubin values were included in the multivariate analysis in Model 1. The ALBI grade was included in the multivariate analysis in Model 2. A p-value of <0.05 was considered statistically significant.

Results: The clinical and demographic characteristics of the patients are shown in Table 1. The relationships of these data with disease-free survival (PFS) and overall survival (OS) is shown in Table 2. High ALBI grades are associated with PFS and OS among the other factors, too (p<0.01). Univariate analysis showed that high ALBI grades indicated poor prognosis in both PFS and OS (HR for PFS: 13.40 (8.5-21.13), p<0.01/HR for OS: 16.23 (10.11-26.06), p<0.01). In the multivariate analyses; both albumin and high bilirubin values alone were associated with PFS and OS in Model 1, predicting the survival prognosis. However, the Model 2 proved that the grade 3 ALBI scores were approximately three times more predictive (HR for PFS: 3.45). (1.98-6.02), p<0.01/HR for OS: 4.41 (2.45-7.93), p<0.01). The results of the other univariate and multivariate analyses are shown in Table 3.

Conclusion: High ALBI grades are much more sensitive than low albumin and high bilirubin levels alone to predict poor prognosis on disease-free survival and overall survival in gastric cancer patients with liver metastasis.

Keywords: ALBI grade, stomach cancer, prognosis

Table 1. Clinical and demographic characteristics of the patients

Parameter	All patients (n=203)
Age (year) Median (Interquartile range)	63 (54-72)
Sex: Male/Female	43/160
ECOG-performance score, n (%) 0-1 >2	96 (47.3) 107 (52.7)
Body-mass index (kg/m ²); n (%) <18.5 18.5-24.9	71 (35.0) 109(53.7)
25.0-29.9 >30.0	21 (10.3) 2(1.0)
HER-2 status, n (%) Positive	37(18.2)
Negative Unknown	83 (40.9) 83 (40.9)
First-line treatment, n (%) Cisplatin + 5-Fluorouracil	5(25)
Cisplatin + 5-Fluorouracil + Trastuzumab Docetaxel+ Cisplatin + 5-Fluorouracil FOLFOX Kapecitabin-Oxaliplatin Supportive treatment	34(16.7) 29(14.3) 52 (25.6) 36(17.7) 47 (23.2)
Serum albumin (g/dL), n (%) <3.5 >3.5	102 (50.2) 101 (49.8)
Serum total bilirubin (g/dL), n (%) <1.2 >1.2	134 (66.0) 69 (34.0)
ALBI grade n (%) Grade l Grade 2 Grade 3	57(28.1) 95 (46.8) 51(25.1)

Table 2. Correlation of the study parameters with progression-free
survival (PFS) and overall survival (OS)

Parameter	Median PFS (95% CI Lower-Upper)	p-value	Median OS (95% CI Lower-Upper)	p-value
Age, year <60 ≥60	5.0 (3.6-6.4) 3.7 (3.1-4.3)	0.06	9.3 (6.1-12.6) 5.4 (3.4-7.3)	0.06
Gender Female Male	4.5 (3.5-5.5) 4.0 (3.1-4.8)	0.12	5.5 (3.9-7.1) 6.8 (4.3-9.2)	0.06
ECOG-performance score 0-1 ≥2	9.1 (7.3-10.8) 2.3 (1.9-2.7)	<0.01	14.3 (12.3-16.3) 2.4 (1.9-2.9)	<0.01
Body-mass index, kg / m2 <18.5 ≥18.5	1.2 (0.6-1.6) 6.9 (5.6-8.2)	<0.01	1.5 (0.8-2.1) 11.5 (9.9-13.2)	<0.01
Her-2 status Positive Negative Unknown	9.8 (5.2-10.7) 6.9 (3.3-5.1) 4.2 (1.7-3.3)	<0.01	12.7 (10.0-15.3) 7.2 (4.3-10.1) 3.0 (1.8-4.2)	<0.01
First line treatment option Chemotherapy Cisplatin + 5-Fluorouracil + Trastuzumab Cisplatin-based (CF and DCF) Oxaliplatin-based (FOLFOX-CapeOX) BSC (no chemotherapy)	5.7 (4.8-6.5) 8.0 (6.0-10.0) 5.0 (3.9-6.1) 5.0 (3.3-6.7) 1.1 (0.5-1.8)	<0.01	9.5 (7.7-11.4) 12.8 (10.2-15.4) 7.2 (4.8-9.5) 9.1 (6.5-11.8) 1.1 (0.5-1.8)	<0.01
Serum albumin, g / dL <3.5 ≥3.5	2.2 (1.7-2.8) 6.9 (5.2-8.6)	<0.01	2.4 (1.8-3.1) 11.6 (9.1-14.0)	<0.01
Serum total bilirubin, g / dL <1.2 ≥1.2	6.0 (5.3-6.7) 1.5 (0.6-2.4)	<0.01	9.8 (8.1-11.4) 1.5 (0.9-2.2)	<0.01
ALBI grade Grade 1 Grade 2 Grade 3	8.9 (6.1-11.6) 4.2 (2.8-5.5) 0.9 (0.7-1.2)	<0.01	14.8 (12.0-17.7) 6.5 (4.7-8.3) 1.0 (0.8-1.2)	<0.01
All patients	4.0 (3.3-4.7)	-	6.4 (4.9-7.8)	



Multivariate (Model 1) Multivariate (Model 2) Multivariate (Model 1) Multivariate (Model 2) Univariate PFS Univariate OS PFS PES 05 05 HR (95% CI Lower limit -Upper limit) HR (95% CI Lower limit -Upper limit) HR (95% CI Lower limit -Upper limit) HR HR HR rik (95% CI Lower limit -Upper limit) rik (95% CI Lower limit -Upper limit) (95% CI Lower limit -Upper limit) p-value p-value p-value p-value p-value p-value Age, year <60 ≥60 Reference Reference Reference Reference Reference Reference 0.06 0.12 0.09 0.03 0.18 0.10 1.31 (0.99-1.75) 1.27 (0.93-1.72) 1.30 (0.95-1.78) 1.36 (1.02-1.82) 1.23 (0.90-1.68) 1.30 (0.95-1.78) Gender Reference Reference Reference Reference Reference Referece 0.13 0.67 0.71 0.07 0.06 0.06 Female Male 0.72 (0.54-11.02) 9.76 (5.60-17.01) 0.76 (0.54-1.08) 0.92 (0.63-1.33) 0.93 (0.64-1.35) 0.70 (0.48-1.02) ECOG Reference 9.38 (6.41-13.72) Reference 4.73 (2.91-7.69) Reference 4.46 (2.74-7.26) Reference 16.86 (10.51-27.04) Referece 9.76 (5.60-17.01) Reference 9.17 (5.22-16.09) < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 0-1 >2 BMI Reference 14.0 (9.25-21.36) Reference 5.12 (3.14-8.34) Reference 11.90 (8.07-17.56) Reference 4.01 (2.48-6.49) Reference 3.81 (2.30-6.29) Reference < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 ≥18.5 <18.5 4.66 (2.82-7.70) HER-2 status Negative / Unknown Positive Reference Reference Reference Reference Reference Reference 0.001 0.47 0.42 0.002 0.33 0.28 0.53 (0.36-0.77) 1.52 (0.47-4.88) 1.60 (0.50-5.13) 1.83 (1.25-2.68) 1.78 (0.55-5.75) 1.89 (0.58-6.12) Chemotherapy Reference 0.18 (0.12-0.27) Reference 0.74 (0.48-1.15) Reference 0.75 (0.48-1.18) Reference 0.12 (0.08-0.17) Reference 0.46 (0.29-0.72) Reference 0.44 (0.28-0.70) < 0.01 0.18 0.21 < 0.01 < 0.01 < 0.01 No Yes Trastuzumah Reference 0.50 (0.34-0.74) Reference 0.48 (0.14-1.62) Reference 0.43 (0.13-1.47) Reference 0.51 (0.34-0.76) Reference 0.40 (0.11-1.38) Reference 0.35 (0.10-1.23) 0.001 0.23 0.001 0.14 0.10 0.18 No Yes Albumin Reference Reference 1.54 (1.07-2.20) Reference 1.70 (1.17-2.47) Reference < 0.01 0.02 < 0.01 0.005 ≥3.5 <3.5 3.16 (2.34-4.26) 3.45 (2.54-4.67) Bilirubin Reference Reference Reference Reference ≤1.2 >1.2 < 0.01 0.007 < 0.01 0.008 -3.32 (2.44-4.53) 3.16 (2.33-4.29) 1.62 (1.13-2.30) 1.65 (1.13-2.39) ALBI grade Reference 2.25 (1.58-3.21) 13.40 (8.5-21.13) Reference 1.86 (1.26-2.74) 3.45 (1.98-6.02) Reference 2.99 (2.03-4.38) 16.23 (10.11-26.06) Reference 2.64 (1.74-3.98) 4.41 (2.45-7.93) < 0.01 <0.01 < 0.01 <0.01 0.01 23 0.01

Table 3. Univariate and multivariate analyses of the study parameters as predictors of survival



Selecting the type of Surgery Based on Premenopausal and Postmenopausal Status: Rationale and a Single Center Experience

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Objective: The aim of this study was to evaluate the correlations of the worldwide published data with the selected types of surgeries and the pre- and postmenopausal status of the patients admitted to the Medical Oncology Clinic, Göztepe Training and Research Hospital, Istanbul Medeniyet University.

Materials-Methods: A total of 436 patients with T1 ve T2 / N0 breast cancer, who were admitted to our healthcare center, were evaluated retrospectively for their premenopausal and postmenopausal status and the selected methods of breast surgery if they had undergone surgery for a unifocal and non-metastatic lesion and if they had received adjuvant/neoadjuvant therapy.

Results: The median age of the study patients was 58 (28-94) years. Of the study patients, 112 (26%) were premenopausal and 324 (74%) were postmenopausal. It was observed that 230 patients had undergone breast conserving surgery (BCS) and 206 patients had undergone mastectomy. BCS was performed in 73 (65%) premenopausal patients and 157 (48%) postmenopausal patients. Modified radical mastectomy (MRM) was performed in 39 (35%) premenopausal patients and in 167 (52%) postmenopausal patients.

Discussion: The results of the meta analyses revealed that there were no differences between the disease-free survival and overall survival when BCS was compared to mastectomy in node-negative breast cancers, while BCS with radiotherapy in node-positive breast cancer was associated with reduced rates of local recurrences compared to mastectomy. A review of the rationale for selecting the type of surgery led to the observation that it depended on patient preferences in our clinic. MKC is associated with lower levels of psychological morbidity; especially with mild severity of anxiety and depression, less impairments in the sex life, and maintenance of the self-esteem. We think that the type of the surgery should be recommended to appropriately selected patients based on the light of our study data.

Keywords: Breast conserving surgery, early stage breast cancer, mastectomy



Evaluation of the Relationship Between the Attachment Styles and Psychological Endurance in Cancer Patients Receiving Chemotherapy

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Introduction: Cancer is considered a traumatic event that may lead to post-traumatic stress disorder. Significant changes occur in the daily life, body image, lifestyle, and social life of the person diagnosed with cancer. Attachment is observed in relationship establishment, seeking closeness, and in the behaviors of a child looking for the caregiver. It is an evolving emotional bond between the child and the caregiver, characterized by continuity and endurance, and comes into force in stressful conditions. The stage of attachment plays an important role in the social lives of adults as well as it does in the lives of children. It was found out that attachment styles are experienced in the relationships during the lifespan of the individuals and they are among the major predictors of psychological endurance. The aim of our study was to investigate the relationship between the psychological endurance and adult attachment styles in cancer patients receiving chemotherapy.

Material-Method: A total of 445 volunteering patients receiving chemotherapy in the medical oncology departments of Dr. A.Y., Ankara Oncology Research and Training Hospital and Ankara Güven Hospital were included in the study after reading and signing the informed consent form for volunteers. The study patients filled in the 'Relationship Scales Questionnaire' and the 'Psychological Endurance Scale for Adults' to assess the attachment styles and psychological endurance, respectively. Because 54 patients could not complete the questionnaire due to several reasons including nausea, pain or time limitations; 391 patients were included in the analysis.

Results: Of the 391 patients included in the study, 285 (73%) were women. The median age of the study patients was 53 (20-83) years. The median endurance score was 130 (49-165). The patients were divided into two groups as the durable and undurable based on the median score. The age, sex, marital status, working status, educational status, economic status of the patients, the people they lived with and they grew up with, their means of their social support, their trust in chemotherapy, and their dominant attachment patterns were compared with an univariate analysis. A multivariate analysis was performed to evaluate the parameters showing statistically differences in the univariate analysis. The multivariate analysis revealed that a moderate or poor social support, lack of trust in chemotherapy; and indifferent or fearful attachment styles were found to be the independent factors acting on the patient's durability.

Conclusion: In conclusion; indifferent and fearful attachment patterns have a significantly negative impact on the durability of patients receiving chemotherapy.

Keywords: Cancer, psychological endurance, secure attachment



The Significance of the Preoperative FDG PET-CT SUV-Max Value on Disease Recurrence in Operated NSCLC Patients

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Introduction: Lung cancer is the most common cause of cancer-related deaths in men and women. Recurrence and metastases develop in most of the patients. Tumor diameter, lymph node involvement, presence of lymphovascular invasion, undergoing sublobar resection, surgical margin positivity, visceral pleural involvement, and presence of perineural invasion are among the prognostic factors1-4. In this study, we aimed to evaluate the predictive significance of the preoperative PET-CT SUV-Max value on recurrence.

Material-Method: Patients with non-small cell lung cancer (NSCLC), who were admitted to the Medical Oncology outpatient clinic of RTE University School of Medicine in the period from 2018 to 2019 were evaluated. Age, the date of diagnosis, type of operation, the tumor diameter, tumor type; presence of visceral pleural involvement, perineural invasion or lymphovascular invasion, grade, surgical margin positivity, perioperative PET CT SUV-max value, history of adjuvant therapy, and any presence of recurrences/metastases were investigated.

Results: Our study included 41 patients and the mean age of the patients was 65.9 (54-82) years. The mean tumor diameter was 3.9 (1.7-8.5) cm. The surgical margins were positive in 1 (2.4%) patient. Lymph node involvement was present in 13 (31.7%) patients. Perineural invasion (PNI) was seen in 6 (14%) patients and lymphovascular invasion (LVI) was seen in 11 (26.8%) patients. A SUV Max value of \geq 10 was found in 26 (63.5%) patients, while a SUV Max value of <10 was present in 15 (36.5%) patients. Seven (17%) patients had a recurrence and 2 (0.4%) patients had metastases. There was a significant correlation between the tumor diameter and the SUV-Max value in the PET-CT imaging (p=0.035).

Discussion: 30% of patients with lung cancer are diagnosed at an early stage5. The main treatment of NSCLC patients in the early stage is surgery. Despite the surgery, recurrence and metastases develop in 55-70% of patients. Studies have shown a relationship between the SUV Max value in PET-CT imaging and disease prognosis in NSCLC patients6-8. In our study, a significant relationship was found between the preoperative SUV Max value and the tumor diameter; however, a significant relationship was not found between the preoperative SUV Max value and local recurrences. Due to the small number of patients included in the study and the short length of the follow-up period, we could not find a relationship of the pre-operative SUV Max values in PET CT with the recurrences and metastases. Larger-scale and more comprehensive studies with long follow-up periods are required.

Keywords: Operated lung cancer, PET-CT, SUV-Max



Autologous Stem Cell Transplantation in Patients with Extragonadal Germ Cell Tumors: A Single Center Experience

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Introduction: Extragonadal germ cell tumors (EGCT) account for 2-5% of all germ cell tumors. The incidence of EGCT is approximately 1/1.000.000. Although EGCT share similar histological, serological and cytogenetic characteristics with gonadal germ cell tumors, their clinical and biological characteristics are different. Chemosensitivity and prognosis is poorer in EGCT compared to gonadal tumors. There is not an established standard salvage chemotherapy regimen for relapsed/refractory EGCT patients. Autologous stem cell transplantation (ASCT) as a salvage treatment for EGCT has recently been on the rise and it is usually performed as a second- or third-line salvage therapy. In this study, we aimed to share our experience with the relapsed/refractory EGCT patients, who underwent ASCT.

Material-Method: A total of 30 patients; who underwent ASCT were selected and included in our study out of the EGCT patients followed up in Gülhane Training and Research Hospital in the period from 1991 to 2018. The patient charts were evaluated retrospectively.

Results: A total of 30 patients were included in the study. The mean age of our patients was 39.5 (21-60) years. While the primary focus was in the retroperitoneum in 20 (66.7%) of our patients, mediastinal tumors were seen in 10 (33.3%) patients. Histopathological tumor characteristics were of the non-seminomatous type. All patients received a first-line BEP chemotherapy of 4 cycles. A retroperitoneal lymph node dissection was performed in 14 patients due to the presence of residual retroperitoneal mass. Because of the relapses in our patients, 27 patients received 3 cycles of TIP therapy and 3 patients received 3 cycles of VIP therapy as the first-line salvage treatment. A complete response was achieved in 10 patients and progression was reported in 5 patients. Thirteen patients received VIP and 2 patients received TIP therapy as the second-line salvage treatment. Complete response was achieved in 6 patients. All patients. AII patients ASCT. In 10 patients, ASCT was used as the second-line salvage treatment. In 20 patients, ASCT was performed as the second-line salvage treatment. Nine of our patients died and 21 of them continued their follow-ups at the time of preparation of this study.

Conclusion: This is the first study to document ASCT experience in patients with EGCT. Although the chemosensitivity and prognosis are poor in EGCT patients compared to patients with gonadal germ cell tumors, their survival is significantly improved with multimodal treatments and ASCT.

Keywords: Autologous stem cell transplantation, extragonadal germ cell tumor, salvage treatment



Factors Affecting Response To Nivolumab in Renal Clear Cell Carcinoma Patients: A Single Center Experience

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Objective: In this study, we aimed to investigate the factors affecting nivolumab response in renal clear cell carcinoma patients.

Material-Method: Twenty-five patients were included; who received nivolumab treatment in the period from 2017 to 2019 in Uludag University, School of Medicine, Department of Medical Oncology. Demographic characteristics of the patients, pathological findings, IMDC (International Metastatic RCC Database Consortium) scores at the time of diagnosis, number of TKIs received before nivolumab therapy, the mean length of TKI treatment before nivolumab therapy, metastatic features before nivolumab therapy, response nivolumab, and factors that may be involved in response to nivolumab treatment were evaluated.

Results: Eighteen out of 25 patients were males and the mean age was 58.1±12.5 years. At the time of diagnosis; 2 patients were at stage 1, 6 patients were at stage 2, and 12 patients were at stage 4. All patients were operated for their primary tumors at the time of diagnosis. The tumor was located on the left side in 15 patients and the right side in 10 patients. Fuhrman grade 2, 3, and 4 were detected in 1, 21, and 3 patients, respectively. In the metastatic stage, 21 patients had visceral metastasis and 4 patients had non-visceral metastasis. At the time of diagnosis; there were 4 poor risk patients, 18 intermediate risk patients, and 3 patients with favorable prognosis based on IMDC risk groups. The mean length of IFN use before nivolumab therapy was 32.5 days and the mean length of TKI use was 24.2 months. Fourteen patients were started nivolumab therapy after one line TKI treatment, 9 patients started nivolumab after 2 lines, and 1 patient started nivolumab treatment after three lines of TKI. One patient started nivolumab therapy after IFN treatment upon obtaining an approval for off-label use. Before the nivolumab therapy, 24 patients had visceral metastases and 1 patient had a non-visceral metastasis. Partial response was observed in 8 patients receiving nivolumab therapy. Three patients had a stable disease; 7 patients had progression, and 7 patients had hyperprogression. The mean PFS was 9.6±1.3 months (CI: 6.9; 12.2). The subgroup analysis demonstrated that; compared to the patients who received more than two lines of TKI treatment, PFS with nivolumab was significantly better in patients, who had received less than two lines of TKI treatment before the nivolumab therapy. Also; compared to the patients with metastasis at the time of diagnosis, PFS with nivolumab was significantly better in the early stage patients at the time of diagnosis; who developed metastases later.

Conclusion: Factors that may be involved in the response to nivolumab therapy in patients with metastatic renal clear cell carcinoma may be examined in larger case studies so that the eligible patients can be identified to start nivolumab treatment earlier.

Keywords: Nivolumab, renal clear cell carcinoma, response



A New Condition in Prognosis in Patients with Metastatic Renal Cell Cancer: The 'Obesity Paradox'

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Introduction: Two models; namely IMDC (International Metastatic RCC Database Consortium) and MSKCC (Memorial Sloan-Kettering Cancer Center) criteria, have been developed to determine the prognosis in patients with metastatic renal cell carcinoma (mRCC). These criteria do not include obesity. However, obesity has been considered a risk factor for the development of renal cell carcinoma. Although obesity is a risk factor for developing RCC, it has been found out that obese patients respond better and show better prognosis in mRCC. This is called the 'obesity paradox'. Our study has investigated the effect of obesity on progression-free survival (PFS) and overall survival (OS) in mRCC patients.

Material-Method: Our study included 100 patients; who were treated for mRCC in Hacettepe University, School of Medicine, Oncology Hospital in the period from 01. January. 2009 to 01. June. 2019. The patients were categorized into two groups as obese and non-obese persons based on their Body Mass Index (BMI) values. Patients with a BMI of ≥30 kg/m² were considered obese.

Results: Our study included 100 mRCC patients to be evaluated. Of these patients, 29% were obese. The demographic characteristics of the patients in our study are shown in Table 1. Obese patients were considered to belong to the very favorable risk group and non-obese patients were considered to belong to the moderate risk group based on their IMDC scores (p=0.04). The median length of PFS in the obese patient group was 390 (75-1323) days and it was 247 (60-900) days in the non-obese patients; demonstrating that the obese patients had longer PFS compared to the non-obese patients (p=0.03, Fig. 1). No intergroup differences were observed in OS (p=0.439).

Conclusion: The effect of obesity on mRCC prognosis has not been fully established. Steffens et al. investigated the relationship of the baseline values of BMI and body surface area (BMI, m²) with prognosis on 116 patients with mRCC. No significant relationships of BMI or body surface area with PFS or OS were observed. In a study on 475 North American patients with RCC, Choueiri et al showed that a higher BMI was associated with longer OS in RCC. In the 100 mRCC patients evaluated in our study, the association of obesity with longer PFS was demonstrated. There were no differences in OS between the obese and nonobese patient groups.

Keywords: Metastatic renal cell carcinoma, obesity, prognosis

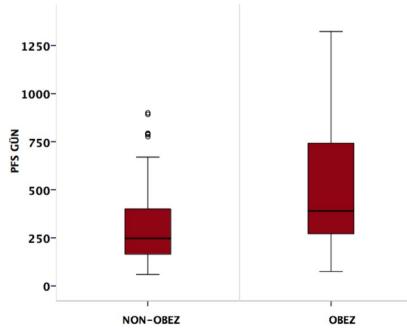


Figure 1. Progression-free survival in obese and non-obese patients

Table 1. Demographic characteristics of the patients

Demographic characteristics	All patients n = 100 (100%)	Obese n = 29 (29%)	Non-obese n = 71 (71%)	p-value
Gender-Male (%)	71 (71%)	14 (48.3%)	57 (80.3%)	
Age*	56 (30-80)	53 (33-73)	57 (30-80)	0.245
Height* (cm)	170 (150-183)	168 (150-181)	170 (155-183)	
Body Weight* (kg)	77 (44-128)	88 (70-128)	73 (44-92)	
Body Mass Index* (kg/m2)	26.45 (16.1-39.5)	31.2 (30-39.51)	25.3 (16.1-28)	
Smoker (%)	58	12 (41%)	46 (64%)	0.03
Risk Group (%) Favorable risk Intermediate risk Poor Risk	30 (30%) 52 (52%) 18 (18%)	16 (55.1%) 9 (31%) 4 (13.8%)	14 (19.7) 43 (60.6%) 14 (19.7%)	0.04
Location (%) Right-side Left-side	49 (49%) 51 (51%)	14 (48.2%) 15 (51.8%)	35 (49.2%) 36 (50.8%)	
Subtype (%) Transparent Papillary Chromophobe Sarcomatoid Mixed Other **	71 (71%) 14 (14%) 3 (3%) 1 (1%) 8 (8%) 3 (3%)	25 (86.2%) 1 (3.4%) 1 (3.4%) 1 (3.4%)	46 (64.8%) 13 (18.3%) 2 (2.8%) 1 (1.4%) 7 (9.9%) 2 (2.8%)	0.05
Number of metastatic regions (%) 1-2 3-4-5	90 (90%) -	29 (100%) •	61 (80.2%) 10 (19.8%)	0.31
Fuhrman Grade (%) 1 2 3 4	6 (6%) 28 (28%) 34 (28%) 32 (32%)	4 (13.8%) 9 (31%) 11 (37.9%) 5 (17.2%)	2 (2.8%) 9 (26.8%) 23 (32.4%) 27 (38%)	0.02
Treatment (%) Pazopanib Sunitinib	54 (54%) 46 (46%)	17 (58.6%) 12 (41.4%)	37 (52.1%) 34 (47.9%)	0.55
Progression-free survival * (days)	266 (60-1323)	390 (75-1323)	247 (60-900)	0.03
Overall Survival * (months)	18.3 (3-104)	24.9 (3-81.4)	16.2 (3-104)	0.439

* Values are given as median and minimum-maximum. ** The section "others" comprises the rhabdoid and translocation types.



The Effect of Neutrophil-Lymphocyte Ratio and Lymphocyte-Monocyte Ratio on the Treatment Response Before Ipilimumab Treatment in Patients with Metastatic Malignant Melanoma

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Introduction: The inflammatory and immunological circumstances in the tumor microenvironment play a critical role in tumor progression and host immune response. Neutrophil-lymphocyte ratio (NLR) and lymphocyte-monocyte ratio (LMR) can be used as both prognostic and predictive factors in determining the immune response. Ipilimumab is a monoclonal antibody that has been shown to prolong survival in patients with metastatic malignant melanoma (MMM). In this study, we investigated the relationship of NLR and LMR with the response rates and survival in MMM patients treated with ipilimumab.

Methods: In this cross-sectional study, the data from 18 patients; who were recorded in the database of Necmettin Erbakan University, Meram School of Medicine, Medical Oncology Department, were evaluated retrospectively. The patients received ipilimumab treatment for the treatment of MMM in the period from November 2012 to September 2019. Demographic data of the patients, NLR, LMR, response rates, progression-free survival (PFS), and overall survival (OS) were analyzed.

Results: Eighteen patients were included in the study. The median age of the patients was 58 years. Ten (55.6%) patients were males and 8 (44.4%) were females. The primary tumor was located in the skin in 14 patients, in the mucosa in 2, and in the uvea in 2 patients. BRAF mutation was detected in 7 (38.9%) patients. Thirteen patients (72.2%) were able to complete 4 cycles of ipilimumab therapy. A stable response was obtained in 8 (44.4%) patients and a partial response was obtained in 2 (11.1%) patients. The median PFS was 3.4 months and the median OS was 24.3 months with the ipilimumab therapy. The mean NLR was lower (1.99 vs 3.6) and the mean LMR was higher (4.13 vs 3.1) in the patients who responded. Grade 1-2 side effects occurred with treatment in 7 (38.9%) patients. During the follow-up period, 11 patients died and 7 patients were surviving.

Conclusion: Our overall survival outcomes with ipilimumab was longer and ipilimumab was better tolerated in MMM patients compared to the information reported in the literature. The high number of patients, who completed 4 cycles of ipilimumab therapy in our study, may be responsible for the longer survival and better tolerability. The effects of baseline NLR and LMR values determined before the treatment were not observed on the objective response or survival rates in our study. The retrospective design of our study and the small number of patients limit the power of our results.

Keywords: Ipilimumab, LMR, metastatic malignant melanoma, NLR



Identification of Cancer Groups, In Which Cachexia Shows Predictive and Prognostic Value

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Objective: Although sarcopenia is known to indicate poor prognosis in cancer patients, its predictive value and significance in different cancer groups have not been clarified. The aim of this study was to analyze the predictive and prognostic value of sarcopenia in different cancer groups.

Methods: Patients, who were followed-up in the Adiyaman Training and Research Hospital's oncology clinic and who received chemotherapy due to the diagnosis of metastatic-stage cancers of the lungs, colon, non-colorectal gastrointestinal system (GIS), breast and the gynecological system, and the prostate were retrospectively included in the study following a consecutive order. The clinicopathological characteristics of the patients were documented. Their pre-chemotherapy muscle mass surface was measured at the level of lumbar-vertebra-3 with computed tomography (CT) (LKK [cm²]). Sarcopenia was analyzed (LKK/ height [m²]) for individual patients. We evaluated the predictive and prognostic significance of the presence of sarcopenia in 5 cancer groups. Categorical data were compared with the chi-square test and non-categorical data were compared with the student t-test. Progression-free survival (PFS) and overall survival (OS) were analyzed with the Kaplan-Meier-method/Coxregression-analysis.

Results: A total of 204 patients were included in the study. Of them, 89 (43.5%) were females. The mean age was 60.7 (±12.7) years. Of the patients included in the study; 18.6% (n=38) had lung cancer, 21.1% (n=43) had colon cancer, 27.0% (n=55) had non-colorectal GIS cancers, 21.6% (n=44) had breast or gynecological cancers, and 6.9% (n=14) had prostate cancer. The median LKK/m2 value was 36.85 for females and 42.0 for males. The values lower than these figures were accepted to indicate sarcopenia. The mean sarcopenia values were listed by the clinicopathological characteristics of the patients in Table 1. The analyses revealed that the female gender and the ages >75 years were the risk factors for sarcopenia. However, the baseline sarcopenia was statistically similar between the groups (Table 1). After adjusting for age; sarcopenia was found to be associated with poor OS only in the breast and gynecologic system cancers (Table 2). In lung and breast-gynecologic system cancers, disease-response-rates were associated with sarcopenia; whereas, no relationships were observed with the GIS and prostate cancers (Table 2).

Conclusion: Our study has demonstrated that sarcopenia has a predictive and prognostic value in the cancers of the breasts and the gynecologic system and the lung cancers. However, these parameters need to be evaluated in larger-scale studies.

Keywords: Cancer, prognostic, predictive, response rate, sarcopenia

 Table 1. Mean sarcopenia values according to the clinicopathological characteristics of the patients

Characteristic	Sarcopenia Median (± SD)	P-value
Age <75 ≥75	40.9 (± 9.7) 34.2 (± 10.6)	0.006
Sex Female Male	36 (± 7.3) 43 (± 10.7)	<0.001
Diagnosis Lung cancer Colorectal cancer Non-colorectal cancers Breast-Gynecological tumors Prostate cancer	$\begin{array}{c} 41.7 (\pm 12.5) \\ 40.4 (\pm 11.1) \\ 38.3 (\pm 8.7) \\ 37.8 (\pm 6.1) \\ 46.7 (\pm 8.9) \end{array}$	0.25
Presence of bone metastases	39.4 (± 9.7) 41.8 (± 10.2)	0.12

SD: Standard Deviation

Table 2. Sarcopenia-associated survival analysis by the patient groups

Diagnosis	Progression-free	Survival			
	HR 95%CI	P-value	Multivariant HR 95% CI	P-valu	
Lung	2.25 (1.06-4.77)	0.035	2.38(1.09-5.16)	0.028	
Colorectal	0.75 (0.37-1.51)	0.41	0.81 (0.38-1.71)	0.57	
Non-colorectal	1.51 (0.85-2.66)	0.15	1.42 (0.79-2.55)	0.24	
Breast-Gynecological System	3.73(1.69-8.21)	0.001	3.49(1.55-7.82)	0.002	
Prostate	1.82 (0.34-9.59)	0.47	1.81 (0.20-11.1)	0.60	
	Overall Surviva	al			
Lung	HR 95% CI 2.02 (0.89-4.57)	P-value 0.09	Multivariant HR 95% CI 2.16(0.94-4.94)	P-value 0.069	
Colorectal	0.93 (0.43-2.17)	0.93	1.02 (0.42-2.47)	0.96	
Non-colorectal	1.52 (0.84-2.76)	0.16	1.29 (0.75-2.59)	0.28	
Breast-Gynecological System	3.23(1.11-9.34)	0.032	4.12 (1.40-12.1)	0.010	
Prostate	0.49		0.18		
	Treatment Res	ponse Rate	es		
	OR 95%CI		P-value		
Lung	2.19(1.07-4.47)		0.028		
Colorectal	1.50 (0.62-3.45)		0.337		
Non-colorectal	1.73(1.01-2.95)		0.063		
Breast-Gynecological System	4.105 (0.67-24.89)		0.016		
Prostate	-		0.400		



Patient Cases With Hyperprogression Due to Nivolumab: A Single Center Experience

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The recent introduction of immunotherapy agents has led to a revolution in cancer treatment, achieving better survival rates in many different cancer types compared to cytotoxic chemotherapy. With the increasing use of immunotherapy, different response patterns such as pseudoprogression and hyperprogression have been described. Pseudoprogression is seen in 2-6% of the patients and it can be described as a transient enlargement of the tumor before a reduction occurs in the tumor size. Hyperprogression (HP) is a paradoxical progression in the tumor growth rate by more than two-folds in patients receiving immunotherapy. Its incidence is reported in the range from 4 to 29%. Increased awareness about this condition and identification of the risk factors are necessary as it is associated with high mortality rates.

Nivolumab has started to be reimbursed in 2017 in our country for its use for the treatment of Hodokin lymphoma, melanoma, and kidney tumors. We evaluated the data of 47 patients, who received nivolumab for advanced stage melanoma and renal cell carcinoma (RCC). We detected 6 (12%) patients; who underwent a radiologic evaluation after nivolumab treatment and who had an increase in the tumor diameter by more than 50%. The clinical characteristics of these patients are listed in Table 1. Five (83%) patients had melanoma and one (17%) patient had RCC. The mean age was 62 (25-85) years. HP was observed after an average of 3.2 (1-4) cycles of nivolumab treatment. Three patients had a history of palliative radiotherapy prior to nivolumab therapy. In all patients with HP, nivolumab was discontinued and supportive therapy was started. It was possible to continue systemic therapy (cisplatin-dacarbazine) only in one patient (Patient A) after nivolumab was discontinued. Other patients were followed up with supportive therapy only because of clinical deterioration after HP.

HP is a treatment response phenomenon and making an early diagnosis in immunotherapy patients is critical in the oncology practice because of the severe morbidity and mortality risks. However, the underlying causes of this phenomenon have not been well described, yet. With the widespread use of immunotherapy, we will encounter HP more frequently. It is important to identify risk factors for these patients.

Keywords: Hyperprogression, immunotherapy, nivolumab

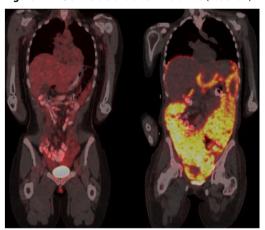


Figure 1. PET/CT before and after nivolumab (Patient A)

Table 1.

PATIENT	A	В	С	D	E	F
SEX	F	F	F	E	E	Е
AGE	25	85	62	77	66	59
DIAGNOSIS	Melanoma	Melanoma	Melanoma	Melanoma	RCC	Melanoma
PREVIOUS TREATMENTS	Ipilimumab, dabrafenib-trametinib	No	Temozolomide	Temozolomide	Interferon, pazopanib	Temozolomide
NİVOLUMAB CYCLES	4	3	1	4	3	4
HISTORY OF RADIOTHERAPY	Brain	No	No	No	Bone	Brain
HYPERPROGRESSION SITE	Lung, peritoneal implants	Lung, liver	Lung	Lung, liver	Brain, liver	Bone, liver, lung
RIGHT / died	Exitus	Exitus	Exitus	Exitus	Exitus	Exitus
Clinical information about the patients.						



Relationship Between Platelet Distribution Width and Tumor Burden in Advanced-Stage Medullary Thyroid Cancers

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Objective: Medullary thyroid cancers (MTC) are rare neuroendocrine tumors. They account for 1-2% of all thyroid cancers. More sensitive and specific evaluation of the tumor volumes have recently been made possible after the increasing use of Ga-68 DOTA-TATE PET/CT. Both calcitonin (Ctn) and carcinoembryonic antigen (CEA) are well-known tumor markers in MTC. In the literature, there are many studies examining the relationship between the platelet distribution range (PDW) and different solid tumors; however, no studies have investigated their relationship with MTC, yet. In this study, we aimed to investigate the relationship between PDW and tumor burden in patients with MTC.

Method: Patients with advanced stage MTC; who were followed-up in the Oncology Clinic of Okmeydan Training and Research Hospital between the years 2017 and 2019, were included in this retrospective study. The whole body metabolic tumor volume (MTV) and the total lesion volume (TLV) were calculated based on the Ga-68 DOTA-TATE PET/CT scan findings of the patients. PDW data were derived from the hemogram results obtained within 2 weeks before the imaging. The Spearman Correlation Test was used for the statistical analysis of the data.

Results: A total of 20 patients; 6 (30%) males and 14 (70%) females were included in the study. The mean age was 52.6 years. Six (30%) of the patients had stage IVA and 14 (70%) had IVC disase. The most common sites of metastases were lymph nodes, bones, and the lungs, respectively. Thirteen (65%) patients were treated with surgery only and 7 (35%) received tyrosine kinase inhibitors for treatment. The mean whole body MTV was 44.9 cm³ and TLV was 249.2. The mean PDW was 13.5 fL. The correlation analysis showed a statistically significant negative correlation between PDW and both the whole-body MTV and TLV (rho=-0.522, p=0.018; rho=-0.602, p=0.005; respectively).

Conclusion: PDW may be considered as a cheaper marker to be used in MTC; however, these data needs to be confirmed by several large-scale studies.

Keywords: Metabolic tumor volume, platelet distribution range, thyroid medullary cancer, total lesion volume



Prognostic Value of GRIm Scores in Pancreatic Cancer

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Objective: Pancreatic cancer is the most fatal tumor of the gastrointestinal tract. The "Gustave Roussy Immune Score" (GRIm score) is a laboratory index developed to best determine the group of patients to receive immunotherapy. Previous studies have demonstrated that the pre-treatment GRIm scores are the independent prognostic factors for OS in patients with non-small cell lung cancer (NSCLC) and renal cell cancer (RCC). In this study, we aimed to determine the prognostic significance of the GRIm score in pancreatic cancer patients.

Method: The demographic and clinical characteristics and the serum laboratory values of the pancreatic adenocarcinoma patients; who had undergone resection surgery and who were followed up in our clinic in the period between December 2007 and July 2019, were retrieved retrospectively. LDH (>248 U/L), albumin (<3.5 g/dl), and neutrophil lymphocyte ratio (NLR) (>6) were used for calculating the GRIm scores. Based on the determined threshold values, each abnormal parameter was attributed one additional point. The patients with GRIm scores of 0-1 were classified as the low-risk group and the patients with GRIm scores of 2-3 were classified as the high-risk group. The data were used in the survival analysis.

Results: A total of 138 patients were included in the study. The median age at the time of diagnosis was 62 years (range: 36-78 years) and the follow-up period was 13.6 months. In the last analysis, 76 (55%) deaths and 109 (79%) disease progression cases were identified. The median OS was 33.2 months (95% CI: 21.94-41.48) and PFS was 12.1 months (95% CI: 9.85-14.52) in the general study group. The median OS was 36.9 months (95% CI: 25.42-48.56) in the group with low GRIm scores and it was 11.1 months (95% CI: 6.83-15.44) in the group with high GRIm scores (p=0.002, Fig. 1). The one-year OS rates were found out to be 85% vs 47% in the low and high GRIm score groups. The two-year OS rates were 64% vs 39% and the three-year OS rates were 53% vs 27%, respectively. The multivariate analysis revealed that advanced age, male gender, presence of diabetes, a tumor diameter 3 cm or larger, an advanced disease stage, and high GRIm scores were the independent factors of poor prognosis (Table 1).

Conclusion: In patients with operated pancreatic cancer, GRIm scores can be used as inexpensive and easily accessible and applicable prognostic markers in the clinical practice. We aimed to investigate the correlations of this laboratory marker with the pathological immune markers in our further studies.

Keywords: GRIm score, neutrophil-to-lymphocyte ratio, pancreas cancer

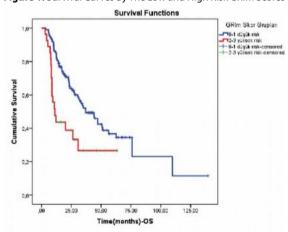


Figure 1. Survival Curves By The Low and High Risk GRIm Scores Table 1

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Factor	Univariate Analysis HR (95% CI)	Univariate Analysis p-value	Multivariate Analysis HR (95% CI)	Multivariate Analysis p-value	
Sex (Males vs Females)	1.29 (0.8-2.07)	0.27	0.46 (0.27-0.79)	0.005	
ECOG (≥2 vs <2)	1.38 (0.7-2.69)	0.33			
Age (≥60 years vs <60 years)	1.37 (0.86-2.17)	0.18	1.87 (1.13-3.11)	0.015	
Smoking status (non-smokers vs smokers or cessated smoking)	1.09 (0.69-1.72)	0.68			
Diabetes mellitus (present vs absent)	1.62 (1.01-2.61)	0.05	1.70 (1.05-2.75)	0.30	
Tumor diameter (≥3 vs <3 cm)	2.22 (1.39-3.55)	0.001	2.20 (1.35-3.57)	0.001	
Stage (2/3 vs 1)	3.17 (1.36-7.38)	0.002	3.48 (1.45-8.35)	0.005	
Surgical margins (positive vs negative)	1.98 (1.24-3.14)	0.004	1.36 (0.81-2.29)	0.23	
GRIm score (high vs low)	2.28 (1.33-3.90)	0.005	2.58 (1.41-4.71)	0.002	

Results From The Univariate and Multivariate Analyses To Determine The Factors Affecting Survival

Grafik1 : GRIm Skorunun Düşük ve Yüksek Risk Sınıflandırmasına Göre Sağkalım Eğrileri



70

Hemoglobin-To-Red Cell Distribution Width Ratio Predicts Survival in Patients with Renal Cell Cancer

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Aim: Hb and red cell distribution width (RDW) are known to be prognostic factors in many cancers. Hb-RDW ratio (HRR) is a new marker that has been shown to have a predictive significance in some cancers. The prognostic significance of HRR in patients with Renal Cell Cancer (RCC) is unknown. In this study, we aimed to investigate the predictive importance of HRR at the time of diagnosis in RCC patients.

Materials-Methods: A total of 198 patients; who were followed-up in our clinic with the diagnosis of RCC in the period from January 2014 to August 2019 and who had no missing data, were retrospectively included in the study. The relationship of the clinical, histopathological, and laboratory parameters with the PFS and OS were analyzed with the Kaplan-Meier curves and compared with the log-rank test. The optimal limits were determined by the ROC curve analysis. Univariate and multivariate analyses were used for determining the prognostic value of the study parameters for PFS and OS.

Results: Neutrophil lymphocyte ratio (NLR), systemic immune inflammation index (SII), HRR, and the lymphocyte-to-monocyte ratio (LMR) were grouped by the defined limit values of 3.86, 1291, 0.72, and 2.43, respectively. A high HRR and LMR were associated with longer PFS (65.38 vs 33.88 months, p=0.000, 55.4 vs 37.6 months, p=0.023; respectively) and longer OS (150.5 vs 135.76 months, p=0.003; 160.7 vs 87.3 months, p=0.001; respectively). A low SII was associated with longer OS (p=0.011). The univariate analysis showed that PFS and OS were significantly related with the Fuhrman Grades; T, N, and disease stages; HRR, and LMR. In the multivariate analysis, it was found out that only the disease stage and HRR were the independent prognostic factors for both PFS and OS (p=0.000, p=0.000; p=0.042, p=0.040; respectively).

Conclusion: In our study, it was shown that a high HRR at the time of diagnosis was associated with longer PFS and OS in the RCC patients. HRR is an easily applicable and inexpensive marker that can be used in the daily practice in this patient group. However, prospective large-scale studies are needed to confirm our results.

Keywords: Hemoglobin, red cell distribution width, renal cell cancer

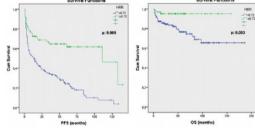


Figure 1. The relationship of HRR with PFS and OS in patients with RCC

the parameters associated with PFS

PFS	Univariate HR	p	Multivariate HR	p
Sex	1.456 (0.989-2.144)	0.057	-	
Age	1.156 (0.816-1.639)	0.41	-	
Pathological Subtype	1.107 (0.741-1.655)	0.61	*	
Fuhrman Grade	3.423 (2.197-5.334)	0.000	1.230 (0.764-1.980)	0.395
Т	3.593 (2.652-4.866)	0.000	0.947 (0.615-1.458)	0.805
N	2.967 (2.034-4.327)	0.000	1.541 (1.055-2.250)	0.025
Stage	3.940 (2.981-5.208)	0.000	3.803 (2.546-5.682)	0.000
NLR	1.268 (0.889-1.903)	0.190	-	
SII	1.329 (0.941-1.878)	0.107	-	
HRR	0.353 (0.226-0.553)	0.000	0.415 (0.262-0.658)	0.000
LMR	0.668 (0.466-0.958)	0.028	0.933 (0.641-1.357)	0.715

Table 1. Univariate and multivariate analysis of Table 2. Univariate and Multivariate Analysis of The Parameters For OS

OS	Univariate HR	р	Multivariate HR	p
Sex	1.080 (0.514-2.270)	0.840	-	
Age	1.329 (0.670-2.634)	0.416	-	
Pathological Subtype	0.715 (0.346-1.477)	0.364	-	
Fuhrman Grade	2.838 (1.160-6.909)	0.022	1.500 (0.590-3.812)	0.394
Т	2.591 (1.499-4.477)	0.001	8.050 (1.862-34.811)	0.005
N	2.100 (1.046-4.216)	0.037	1.208 (0.589-2.571)	0.624
Stage	1.708 (1.124-2.595)	0.012	0.250 (0.066-0.951)	0.042
NLR	1.444 (0.710-2.938)	0.311	-	
SII	2.433 (1.194-4.956)	0.014	1.431 (0.592-3.466)	0.426
HRR	0.203 (0.062-0.664)	0.008	0.282 (0.084-0.942)	0.040
LMR	0.335 (0.165-0.679)	0.002	0.425 (0.176-1.025)	0.057

index. HRR: Hb-to-RDW ratio. LMR: Lymphocyte-to-monocyte ratio



Survival Data and Prognostic Factors in HER2/Neu Positive Metastatic Breast Cancer Patients Undergoing TDM1: A Single Center Experience

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Objective: Ado-trastuzumab emtansine (TDM1) is a combined treatment agent comprising the antitumor agent emtansine (DM1) and trastuzumab (T), a monoclonal antibody targeting human epidermal growth factor 2 (HER2/neu) antigen. This treatment is started in Her2/neu positive metastatic breast cancer patients in the first line and continued in further lines during the course of treatment. We aimed to present the survival data and the respective prognostic factors in patients treated with TDM1 in our center.

Methods: The data of the patients; who were diagnosed with invasive breast carcinoma in the period from 2006 to 2018 and who were treated with TDM-1, were retrospectively reviewed. The age of the patents, their menopausal status, tumor histology and molecular characteristics, the date of diagnosis and the date of detection of metastatic disease, any presence of visceral metastasis at the time of starting TDM1 therapy, and the treatments received by the patients were retrieved. The data were analyzed using SPSS.

Results: Thirty-four patients were included in the study. The median age was 55 years. Fifteen (44%) patients were postmenopausal and 19 (56%) were premenopausal. Hormone receptors (HR) were positive in 20 (58.8%) patients. Surgical resection was performed in 19 (55.8%) patients. Ten (29.4%) patients received neoadjuvant chemotherapy, 15 (44.1%) received adjuvant chemotherapy, and 14 (41.2%) received adjuvant radiotherapy. At the time of starting TDM-1 therapy, 22 (64.7%) patients had visceral metastasis. TDM-1 was administered in the first line in three (8.8%) patients, in the second line in 11 (32.3%) patients, and in the third or higher lines in 20 (58.8%). Fourteen (41.2%) patients received at least one cycle of treatment after TDM-1. TDM-1-associated PFS and OS were 6.3 months (95% CI, NR-7.8) and 24.2 months (95% CI; NR-36.5), respectively. OS was significantly superior in the premenopausal patients compared to the postmenopausal patients (p = 0.02); however, no significant intergroup differences in PFS were detected. Analyses of HR positivity and the presence of visceral metastases did not reveal any statistically significant differences in PFS or OS. The relationship of treatment continuation after TDM1 was not significantly related with OS. PFS and OS were superior in the patients receiving 3rd-line and further TDM1 therapy compared to the patients receiving TDM1 in the second line; however, the differences were not statistically significant.

Conclusion: In line with the information in the literature, TDM1 is efficacious when used in the third line and further. The differences in the tumor biology in individual patients may be the reason for superior survival outcomes in the patients receiving TDM1 after the third line. PFS was found to be shorter than the reported length in the literature in the patients, who received TDM1 in the second line. This might have occurred due to the limited size of the study sample.

Keywords: Breast cancer, survival, TDM-1

	n	PFS (months)	95% Confidence Interval	р	OS (months)	95% Confidence Interval	р
Menopausal status Premenopausal Postmenopausal	22 12	7.2 6.3	4.6-9.9 1.5-11.0	0.19	28.2 9.9	28.2 9.9	0.02
Hormone Receptor Positive Negative	20 14	6.1 8.2	0.0-12.7 5.0-11.4	0.25	25.2 9.9	22.1-28.3 7.7-12.1	0.23
Visceral Metastasis Yes No	22 12	5.4 7.9	1.4-9.3 6.1-9.7	0.29	20.9 28.2	3.5-38.2 NR	0.29
TDM-1 Use 2nd-line 3rd-line and over	11 20	2.9 7.9	NR-3.2 NR-10.0	0.29	9.4 20.9	NR-24.3 NR-37.1	0.29

Table 1. Survival Outcomes

Table 2.	Treatments	After TDM-1
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	n	OS (months)	95% Confidence Interval	p
Treatments after TDM-1 Yes No	14 20	24.2 16.0	NR 18.4-30	0.76



Factors Predicting Survival in our Patients with Thyroid Cancer

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Objective: Thyroid cancer (TC) accounts for 1% of all cancer types and it is the most common endocrine tumor. It is 2-3 times more common in women than in men with increasing incidence in both sexes in recent years. Although this type of tumors are associated with low mortality rates and favorable prognosis, survival rates vary depending on several factors. We aimed to demonstrate the factors that predict the length of survival in our TC patients, who were followed-up in our clinic.

Methods: Seventy patients, diagnosed with TC in the period from 2005 to 2019 in Atatürk University Medical Oncology Clinic, were included in this study retrospectively. The relationship of the clinic-demographic parameters with the overall survival (OS) and progression-free survival (PFS) were analyzed with the Kaplan-Meier curves and compared with the log-rank test.

Results: The median age was 57.5 (20-76) years in our patients. Of the patients, 38 were women. According to histological subtypes, papillary carcinoma was the most common (n=41, 58.6%). According to the TNM system, stage 1 patients were the most common (n=25, 35.7%). Negative margins were achieved in 56 out of 62 patients; who underwent surgery. Capsular, lymphovascular, and extrathyroidal invasion was found in 50, 38, and 20 patients, respectively. The most common location for metastases was the lung (n=12, 63.2%). Radioactive iodine treatment and sorafenib were administered to 44 and 17 patients, respectively. The median length of follow-up period was 43 (1-169) months. At the end of this period, 45 of our patients progressed and 28 died. The median lengths of PFS and OS in these patients were 41 and 117 months. While the presence of lymphovascular and extrathyroidal invasion were associated with shorter PFS; there were statistically significant differences in PFS and OS between the patient groups formed based on age, ECOG performance scores, TNM stages, surgical treatment and margins, and the tumor size (Table 1).

Conclusion: Although life expectancy in TC is long in general, the histologic subtype and the age at the time of diagnosis are the critical prognostic factors. Additionally; sex, tumor size, and the metastatic site are associated with changes in survival. In line with the literature, both PFS and OS were found out to be longer in younger patients (<55), at early stages, in well-differentiated tumors (papillary-follicular), and in small-sized (4 cm) tumors in our study.

Keywords: Age, prognostic factors, stage, thyroid cancer

					PFS			OS	
		Total (n)	Total (%)	Mean	Median	р	Mean	Median	р
Age	<55	30	42.9	122.7		< 0.001	144.6		<0.00
	≥55	40	57.1	32.9	13		65.5	61	
ECOG	0-1	56	80	74.6	41	0.032	112.1		0.007
	2	14	20	34.9	13		58.3	66	
Histological subtype	Papillary	41	58.6	79.3	61	0.008	107.3	117	0.001
	Follicular	10	14.3	73.2	54		119.8		
	Medullary	11	15.7	37.1	26		80.3		
	Anaplastic	8	11.8	20.5	7		29.2	9	
TNM Stage	1	25	35.7	135.5		< 0.001	151.3		<0.00
	2	19	27.1	48.8	41		93.1	117	
	3	3	4.3	51.6	61		86	61	
	4	23	32.9	20.4	9		44.2	20	
Surgery	Yes	62	88.6	73	50	< 0.001	110.7	129	<0.00
	No	8	11.4	13.1	8		21.6	9	
Surgical margins	Negative	56	90.3	79.2	54	0.006	116.7		0.004
	Positive	6	9.7	23.1	2		35.5	5	
Tumor size	<4 cm	36	51,4	107		< 0.001	138.9		<0.00
	≥4cm	34	48.6	28.7	12		62.1	61	
Lymphovascular invasion	No	24	38.7	92.4	119	0.023	117.6		0.178
	Yes	38	61.3	58.4	36		101.5	117	
Extrathyroidal invasion	No	42	67.7	90.7	71	0.020	120.3		0.176
	Yes	20	32.3	41.3	36		80.8	66	

Table 1. Overall survival and progression-free survival according to the clinical, demographic, and pathological features

PFS: Progression-free survival, OS: Overall surviva



Are Neutrophil/Lymphocyte Ratio and Platelet Distribution Width Predictors of Invasion In Bladder Carcinoma?

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Introduction: Bladder cancer is a common type of malignancy and 15-25% of urothelial carcinomas are invasive. Intracavitary BCG therapy is one of the options for prophylaxis and treatment. One anti-tumor mechanism of BCG is associated with the local immunological responses in urothelial cells. Inflammatory cells around tumor cells play an important role in the disease progression and prognosis.

Material: For this retrospective study, we reviewed the pathological examination reports of 250 patients with urothelial cancer diagnosed in the period from 2013 to 2019. Blood samples were collected before surgery for complete blood count tests.

Results: The study population comprised three groups; namely the muscle-invasive urothelial tumor group (n=107), non-muscle-invasive urothelial tumor group (n=143), and the group of healthy individuals (n=150). NLR had the most significant p-value in relation to the pathological stage (p=0.005), whereas platelet counts were associated with the highest risk (OR=4.2746). The risk ratios of these parameters are listed from the most robust one to the poorest consecutively as follows: Platelet counts >PD >female gender >NLR >age (OR values in the respective order: 4.2746-4.1254-3.9734-2.8787-2.5434). The lymphocyte count was increased in 78% of the non-muscle invasive patients and 45% of the muscle-invasive patients. Healthy individuals with high NLR have significantly lower NK activity compared to those with a low NLR. The platelet count was found out to be significantly correlated with the tumor size, tumor stage, and the condition of the surgical margins (p=0.038-0.042-0.031, respectively). Leukocyte count is an easy procedure to predict the cancer prognosis conveniently. Thrombocytosis may adversely affect the survival by facilitating cell invasion and metastasis. There is evidence that platelets protect tumor cells from the host's immune system.

Keywords: Neutrophil/lymphocyte ratio, urothelial carcinoma, platelet distribution width



The Role of 68Ga PSMA PET-CT in the Evaluation of Late Treatment Response in Patients Receiving Second-Generation Anti-Androgen Therapy for Metastatic Prostate Cancer

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Objective: The aim of this study was to investigate the necessity of 68Ga PSMA PET-CT imaging to evaluate the late (>3 months) treatment response in metastatic prostate cancer patients receiving second-generation antiandrogen therapy.

Methods: The study included 11 patients who were treated with second generation antiandrogen (enzalutamide or abiraterone) for metastatic prostate cancer in the period from March 2018 to April 2019. The inclusion criterion was undergoing 68Ga PSMA PET-CT imaging maximum 15 days before and at least 3 months after the treatment to evaluate the treatment response. The treatment response was evaluated by comparing the serum PSA levels before and after treatment. The obtained results were then compared with the 68Ga PSMA PET-CT imaging findings.

Results: The mean age of the patients was 69.6 (57-83) years. Four patients received abiraterone and seven patients received enzalutamide. The mean time from the initial diagnosis to the onset of treatment was 73.5 (4-163) months. 68Ga PSMA PET-CT imaging was performed on average in the 6.6 (4-13) month after the treatment start. The mean serum PSA values of the patients were 35.57 (0.13-212.03) ng/ml before the treatment and 395.72 (0.23-2386.65) ng/ml after the treatment. Comparisons of the pre-treatment period with the post-treatment period revealed that a significant increase in the serum PSA levels occurred in 8 patients, a decrease occurred in the PSA levels in 2 patients, and stable PSA levels were maintained in 1 patient. Based on the 68Ga PSMA PET-CT imaging findings, 8 patients had progression and 2 patients had a partial response, while 1 patient had a stable disease course. These results were found out to be correlated with the results of treatment response evaluation based on the serum PSA levels.

Conclusion: 68Ga PSMA PET-CT imaging does not additionally contribute to the clinical evaluation of the late (>3 months) treatment response in patients receiving second-generation antiandrogen therapy for metastatic prostate cancer, excluding exceptional cases which may benefit from the correlation of the results with the serum PSA levels.

Keywords: Anti-androgen treatment, prostate cancer, 68 Ga-PSMA PET/CT



The Effect of Treatment Options on Survival in Geriatric Patients with Locally Advanced Non-Small Cell Lung Cancer

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Introduction: The aim of this study was to retrospectively investigate the effect of treatment options on survival in 70-year-old or older patients with non-operated locally advanced non-small cell lung cancer (NSCLC).

Methods: The study included 70-year-old or older patients; who were diagnosed with locally advanced non-small cell lung cancer (NSCLC) in the period from 2005 to 2017, who did not undergo operation for the treatment of NSCLC, who were not diagnosed with any other types of cancer but the NSCLC, and who had no missing data. A total of 2259 patients were retro-spectively reviewed using the information in the patient charts. A total of 130 patients were included in the study. The patients were assigned to four study groups based on the treatment modalities they had received. These study groups were the chemotherapy (CT), concurrent chemoradiotherapy (CCRT), sequential chemoradiotherapy (SCRT), and radiotherapy (RT).

Results: Of the 130 patients included in the study; 25 (19.2%) had receive CT, 30 (23.1%) had received CCRT, 31 (23.8%) had received SCRT, and 44 (33.8%) had received RT. Of the study patients, 12 (9.2%) were females. The median age was 72 years (range: 70-88). There were 60 (46.2%) stage IIIA patients and 70 (53.8%) stage IIIB patients. The median length of progression-free survival (mPFS) was 8.0 months in CT patients, it was 15 months in the CCRT patients, 10.0 months in the SCRT patients, and 9.0 months in the RT patients (Log rank; p=0.07). The median length of overall survival (mOS) was 10.0 months in CT patients, it was 33.0 months in the CCRT patients, and 15.0 months in the RT patients (Log rank; p=0.04). The multivariate analysis revealed that ECOG PS of 2 (HR, 2.10) and 3-4 (HR, 5.13) and stage IIIB (HR, 2.8) tumors were the factors acting on the survival rates unfavorably. However, CCRT (HR, 0.45) and SCRT (HR, 0.50) were found out to affect the survival rates favorably.

Discussion: The use of combined treatment modalities significantly improved survival in our study. The best rates of survival were achieved in the patients treated with CCRT. We suggest that CCRT should be recommended for the treatment of inoperable stage III NSCLC patients over 70 years old.

Keywords: Chemoradiotherapy, geriatric, lung cancer

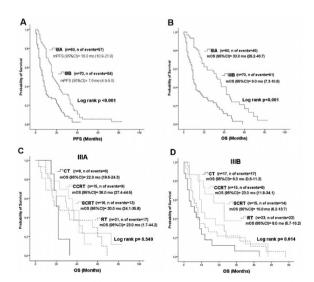


Figure 1. Survival by the disease stage, PFS (A) and OS (B) by the disease stage, OS (C) by the treatment group in stage IIIA disease, OS (D) by the treatment group in stage IIIB disease.



The Role of Exosomal Survivin in the Diagnosis of Breast Cancer

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Introduction: Breast cancer is a major public health problem for women in the world. Early diagnosis, identifying the patients that will benefit from neoadjuvant or adjuvant therapy, and determining the risk of recurrence for an individual patient are critical factors that will improve the survival rates. Exosomes and exosomal survivin continue to receive more insight for their roles in the carcinogenesis. The aim of this study was to determine the relationship of exosomes and exosomal survivin with the breast cancer.

Methods and Patients: Patients; who were followed up with histopathologically confirmed breast cancer in the Medical Oncology Clinic of Medicalpark Gaziantep Hospital in the period from 2014 to 2017 and healthy volunteers were included in the study. Serum samples were collected from the patients and healthy volunteers and they were stored at -80. Exosomes were isolated from these serum samples. The isolated exosomes were disintegrated. Survivin levels were measured by the Enzyme Linked Immunosorbent Assay (ELISA) method.

Results: A total of 75 participants were included in the study. Of them, 55 were breast cancer patients and 20 were healthy volunteers. The exosomal survivin levels were significantly different between the patient and control groups (p=0.047). The mean exosomal survivin level was 2.48 \pm 6.38 ng/mL (Range: 0-40.452) in the patient group and 0.23 \pm 0.52 ng/mL (Range: 0-2.4) in the control group. The difference between the two groups was investigated by the Mann-Whitney U test. There was a statistically significant difference between the breast cancer patients and the control group (p=0.037). The exosomal survivin levels were not correlated with the other prognostic clinicopathological indicators.

Discussion and Conclusion: Survivin was previously shown to be a prognostic marker in breast cancer patients, indicating poor prognosis. The expression of survivin has been shown to occur via the exosomal pathway. Exosomal survivin expression is higher in breast cancer patients compared to the control group. The exosomal pathway may prove to be both a target for treatment and a new marker for making an early diagnosis of the disease.

Keywords: Breast cancer, diagnosis, exosome, survivin

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