Poster Session 1: Basic 1

P1 – 001 SRPX2 IS A NOVEL CHONDROITIN SULFATE PROTEOGLYCAN THAT IS OVEREXPRESSED IN GASTROINTESTINAL CANCER
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SRPX2 (Sushi repeat-containing protein, X-linked 2) has recently emerged as a multifunctional protein that is involved in seizure disorders, angiogenesis and cellular adhesion. Here, we analyzed this protein biochemically. SRPX2 protein was secreted with a highly post-translational modification. Chondroitinase ABC treatment completely decreased the molecular mass of purified SRPX2 protein to its predicted size, whereas heparinase, keratanase and hyaluronidase did not. Secreted SRPX2 protein was also detected using an anti-chondroitin sulfate antibody. These results indicate that SRPX2 is a novel chondroitin sulfate proteoglycan (CSPG). Furthermore, a binding assay revealed that hepatocyte growth factor dose-dependently binds to SRPX2 protein, and a ligand–glycosaminoglycans interaction was speculated to be likely in proteoglycans. Regarding its molecular architecture, SRPX2 has sushi repeat modules similar to four other CSPGs/lecticans; however, the molecular architecture of SRPX2 seems to be quite different from that of the lecticans. Taken together, we found that SRPX2 is a novel CSPG that is overexpressed in gastrointestinal cancer cells. Our findings provide key glyco-biological insight into SRPX2 in cancer cells and demonstrate that SRPX2 is a novel cancer-related proteoglycan family.

P1 – 004 FUNCTIONAL ANALYSIS OF REPRIMO AS A SUPPRESSOR GENE IN GASTRIC CANCER
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Background: Reprimo was demonstrated to be a highly glycosylated protein, inducing cell cycle G2 arrest. Reprimo promoter methylation has been also reported as the mechanism regulating its expression in gastric cancer, but the biological roles largely remain unclear.

Methods: The methylation status of the Reprimo promoter was analyzed using quantitative methylation-specific polymerase chain reaction, and the effects of expression were examined using Reprimo stable transfection.

Results: Reprimo expression was induced by DNA damaging treatment in cell lines with its hypermethylation, but not those with its hypomethylation, in that Reprimo expression could be restored by treatment with a demethylating agent. Exogenous Reprimo protein was also detected using an anti-chondroitin sulfate antibody. These results indicate that Reprimo is a novel chondroitin sulfate proteoglycan (CSPG).

Conclusion: Reprimo expression is inducible under DNA damaging agents, leading to decreased growth, but its expression is frequently suppressed by promoter methylation. Thus, Reprimo methylation status is considered to have a great potential as a predictive biomarker to select patients who may be effective for anticancer therapy in gastric cancer.

P1 – 005 EFFECT OF FORMALIN FIXATION ON IMMUNOHISTOCHEMICAL STAINING FOR HER2
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Background: Assessing HER2 status accurately and reliably is of great importance in optimizing treatment of HER2-positive breast or gastric cancer. In gastric cancer, for which trastuzumab treatment has been recently approved in Japan, immunohistochemistry (IHC) is the standard method for evaluating the HER2 level.

In this study, we examined the impact of formalin fixation conditions on HER2 staining using xenografted tumor samples from mouse models.

Methods: Mice (BALB/c-nu) were subcutaneously inoculated with two human gastric cancer cell lines, SCH (score 2+) and SNU-16 (score 1+). Xenograft tumor tissues were collected and left at room temperature for 0, 6 or 24 h before being fixed with 10% neutral buffered formalin for 24 h, 5, 7 or 10 days and then embedded in paraffin. To examine the effect of fixing solution on HER2 IHC, we used 10% neutral-buffered or non-buffered formalin or Ufix (Sakura Finetek Japan). HER2 IHC was carried out according to the Hercep test. We assessed the effect on IHC by examining the atrophy of tumor cells, autolysis of tumor tissues, immunostaining intensity and immunostaining area.

Results: Continuous staining of HER2 on the cell membrane with moderate intensity was observed in SCH tumors, whereas partly localized staining on the cell membrane with weak immunostaining intensity was seen in SNU-16. Leaving samples for 6 h before fixation at room temperature decreased immunostaining intensity and induced atrophy of peripheral tumor tissues in both SCH and SNU-16 specimens. Leaving the specimens for 24 h before fixation induced autolysis of tumor tissues and reduced the immunostaining intensity. On the other hand, fixation in 10% neutral buffered formalin for more than 5 days diminished the HER2-stained area in SNU-16 samples. Fixing in 20% neutral buffered or in 10 or 20% non-buffered formalin reduced the staining intensity by prolonged fixation. Ufix did not influence the staining area, but atrophied the tumor cells.

Conclusion: Our results suggest that the timing of fixation, including when it starts and how long it takes, will influence the HER2 staining. Non-buffered or highly concentrated formalin also might affect the IHC result. It is important to optimize the conditions of sample collection and fixation.

P1 – 007 EXTRACELLULAR MATRIX INDUCES MESENCHYMAL-TO-EPITHELIAL TRANSITION IN KM-H2
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Background: Hodgkin Reed–Sternberg (H-RS) cell is the tumor cell of classical Hodgkin disease (cHD), and their characteristics are still unclear. KM-H2 was established as an H-RS cell line from pleural effusion of a patient with cHD. We investigated the implications of extracellular matrix (ECM) for adhesion and function of H-RS cell.

Methods: Adhesion assay was carried out with the in situ crystal violet staining method. Cell staining was carried out using monoclonal antibodies conjugated with fluoro-dye. Stained cells were analyzed by a FACScan.

Results: We seeded KM-H2 onto the gelatin-coated or non-coated dish. KM-H2 cultured on a non-coated dish grown as a floating cell and formed a cell cluster (referred to hereafter as fl-KM-H2). However, KM-H2 tightly adhered onto the surface of dish and achieved cell spreading following cultivation on a gelatin-coated dish for 24 h (referred to hereafter as ad-KM-H2). When KM-H2 was cultured on a gelatin-coated well, the significant increase of the number of the adhesive cell was observed. Moreover, ad-KM-H2 abundantly expressed E-cadherin whereas fl-KM-H2 lacked the expression of E-cadherin. Because E-cadherin was widely accepted hallmark of mesenchymal-to-epithelial transition (MET), we concluded that gelatin could promote MET in KM-H2.

Conclusion: ECM components could induce MET in KM-H2. Further investigation might become a milestone to explore an alternative molecular target for antitumor therapy.

Poster Session 2: Basic 2

P1 – 009 EFFECT OF OLIGODEOXYNUCLEOTIDES EXPRESSING A POLY-G MOTIF ON ANTI-TUMOR IMMUNITY
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Previous studies established that immunostimulatory oligonucleotides (ODN) expressing CpG motifs trigger cells that express TLR9, activating an innate immune system response that can slow tumor growth. There are several classes of CpG ODN,
and we examined the activity of the less well-studied 'D' (also referred to as 'A') class ODN. 'D' ODN are characterized by two features: (i) the CpG motif is expressed on a stem-loop structure and (ii) a poly-G tail is present at the 3′-end. In studies of CT26 colon cancer cells, we found that intratumor injection of 'D' ODN elicited strong anti-tumor activity. Unexpectedly, control ODN lacking a CpG motif but expressing a poly-G tail also slowed tumor progression whereas ODN lacking both the CpG motif and poly-G tail were inactive. The anti-tumor activity of ODN expressing a poly-G tail was TLR9 independent, as it was persistently involved in TLR9 KO mice. This anti-tumor effect of poly-G containing ODN was abrogated by depletion of CD8 T cell in vivo, and the treatment with this ODN generated strong tumor cellular responses against tumor. By antigen presentation assay, we demonstrated that poly-G ODN enhanced acquired immunity. For mechanistic understanding, the production of IL-2 from TLR9 knockout spleen cells were demonstrated that poly-G ODN enhanced acquired immunity. For mechanistic understanding, the production of IL-2 from TLR9 knockout spleen cells were demonstrated that poly-G ODN enhanced acquired immunity.

Background: The PI3K/AKT pathway plays a pivotal role in hepatocellular carcinoma (HCC). Mutant PIK3CA, encoding the p110α catalytic subunit, stimulates the AKT pathway and promotes cell growth in various cancers. PIK3CA mutations have been researched in many cancer types and the mutation rate varies in HCC, which was reported in most studies with low frequency (<5%) except one report from Korea (35.6%). Therefore, we confirmed the frequency of PIK3CA mutation in Korean HCC patients.

Methods: We sequenced the exons 1, 3, 4, 6, 7, 8, 9, 19 and 20 of PIK3CA in 268 HCC tumor tissues. Results: In this experiment, the mutations were not detected in exons 3, 6, 8 and 19 and detected 1 of 268 at unknown SNP (G275A) in exon 1 and at unknown SNP (C848G) in exon 4, 1 of 265 at unknown SNP (C1373A) in exon 7, each of 262 at unknown SNP (T2970A) and SNP (G3026A) in exon 20. However, 1 of 266 was detected at unknown SNP (C1629T), 1 each of 262 at unknown SNP (T2970A) and SNP (C1373A) in exon 7, each of 262 at unknown SNP (T2970A) and SNP (G3026A) in exon 20. Conclusion: PIK3CA mutations in hepatocellular carcinoma (HCC) are not common.

Results: Our results showed that levels of acetyl-tubulin, α-tubulin, β-tubulin, γ-tubulin and tubulin were significantly higher expression in PC3/DX than in parental PC3 cells by western blotting analysis. PC/DX with greater resistance to docetaxel had higher levels of acetyl-tubulin than in PC3 cells. The expression of acetyl-tubulin was gradually increased by docetaxel in a dose- and time-dependent manner in both PC3 and PC3 cells. Histone deacetylase 6, a deacetyl enzyme of tubulin, mRNA and protein levels were significantly decreased in PC3/DX than in PC3 cells. Interestingly, we also found an evident up-regulation of acetyl-tubulin protein expression after recombinant epidermal growth factor treatment in a time-dependent manner in PC3/DX cells.

Conclusions: Up-regulation of acetyl-tubulin may play an important chemoresistant role in docetaxel-resistant prostate cancer.

PIK3CA MUTATIONS IN HEPATOCELLULAR CARCINOMA IN KOREA

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Core message: PIK3CA mutations in hepatocellular carcinoma (HCC) are not common.

Influence of CYP1A2, CYP3A5 and CYP2C19 polymorphisms on imatinib mesylate drug responses in three major Asian ethnic groups and variation of im and active metabolite (M1) trough level among chronic myeloid leukemia patients

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Background: Imatinib mesylate (IM) is the first-line treatment and gold standard for treatment of chronic myeloid leukemia (CML). Pharmacokinetic profile of IM and its active metabolite, N-desmethylinatinib (M1) in CML patients are clinically important.

Objectives: This study aimed to determine the influence of CYP1A2, CYP3A5 and CYP2C19 polymorphisms on the drug response of IM in Asian CML. We also aimed to determine the pharmacokinetic profile for both IM and M1 in CML patients with prescription 400 mg PO.

Methodology: A total of 250 healthy volunteers (controls) and 50 CML patients (cases) receiving IM were enrolled in a prospective pharmacogenetic study. CYP1A2, CYP3A5 and CYP2C19 polymorphisms were genotyped in both control and case groups using PCR-RFLP. In the pharmacokinetic study, serum IM and M1 concentrations were measured using the validated ultra-high performance liquid chromatography method on first three CML patients with 400 mg IM PO. The χ² test is used to correlate CYP1A2, CYP3A5 and CYP2C19 genotypes to good responder and resistant group.

Results: The genotype frequencies of CYP1A2, CYP3A5 and CYP2C19 SNP will be observed high standard deviation (>20% of mean) in volume of distributions (Vd), clearance (CL) and area under curve (AUC) for both IM and M1. For IM,
Activin-A is a homodimeric protein consisting of two INHBA (innhibin βA subunit) and belongs to the large transforming growth factor β (TGF-β) superfamily. In cancer, it is known that activin-A is overexpressed in various cancers such as esophageal, pancreatic and ovarian cancers; however, their involvement in angiogenesis remains largely unclear. Our microarray analysis for the clinical specimen of gastric cancer revealed that the mRNA expression of INHBA was overexpressed in several cancer cell lines. Secreted activin-A protein was also confirmed by ELISA and the concentration varied markedly by individual cell lines. Activin-A and TGF-β directly inhibited the cell growth of HUVEC (human umbilical vascular endothelial cells) in a dose-dependent manner. Both activin-A and TGF-β increased the phosphorylation levels of smad on HUVEC cells, suggesting that the TGF-β signal pathway actually functioned in HUVEC cells. Flowcytometry revealed that activin-A and TGF-β induced cell cycle arrest in HUVEC cells. These results suggest that activin-A has a growth inhibitory effect on the vascular endothelial cell and the overexpression of activin-A in gastric cancer may contribute anti-angiogenic roles for tumor growth.

**Poster Session 3: Lung cancer NSCLC 1**

**A PHASE I/II TRIAL OF ERLOTINIB S-1 THERAPY IN PATIENTS WITH PREVIOUSLY TREATED NON-SMALL-CELL LUNG CANCER: THORACIC ONCOLOGY RESEARCH GROUP (TORC) 0808/0913**

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**Background:** Synergistic effects of gefitinib used in combination with S-1 have been reported because of a reduction in the expression of thymidilate synthase in use of gefitinib. Erlotinib also reduced TS expression and activity. The present studies were carried out a retrospective analysis of patients who received treatment with S-1 after the standard treatment of non-small cell lung cancer. They are already treated with guideline recommended chemotherapy regimens. We carried out a retrospective analysis of patients who received treatment with S-1 80 mg/m2 (d1–28) or S-1 80 mg/m2 (d1–14) and CBDCA AUC 5 (d1). Results: From April 2010 through February 2012, five patients were received therapy with S-1 and four with CBDCA + S-1. The disease control rate after 12 weeks was 89%, but there were no PR. The main toxicity was myelosuppression, gastrointestinal disorders. One case of grade 4 mucosal damage, one case of grade 3 diarrhea and one case of grade 3 thrombocytopenia were observed. Other adverse events were mild and could be tolerated.

**Conclusion:** Concerning patients with a good PS at the time of disease progression, chemotherapy using S-1 may be associated with a good disease control rate and an acceptable toxicity in spite of finishing guideline recommended chemotherapy. The prospective study for third- or fourth-line chemotherapy with S-1 should be considered.

**Poster Session 4: Lung cancer NSCLC 2**

**FIRST-LINE CHEMOTHERAPY WITH CARBOPlatin AND DOCTAXEL FOR ADVANCED SQUAMOUS CELL LUNG CANCER**


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The efficacy and toxicity of treatment with carboplatin (AUC = 5) + docetaxel (70 mg/m²) were analyzed retrospectively in 22 patients with advanced squamous cell lung cancer. The median age of the patients was 67 years (range: 56–83 years). The performance status (ECOG) and the clinical stage in the patients were as follows: PS: 0, 11 patients; PS 1, 11 patients; disease stage: stage IIIA, 3 patients; stage IIIB, 6 patients; stage IV, 13 patients. The median number of treatment cycles administered was 4. The median survival time was 10.5 months and the 1-year survival rate was 43.8%. The response rate was 45.4%. The major toxicities were leukopenia and neutropenia; grade 3/4 neutropenia occurred in 19 patients (86.4%). Common toxicities included grade 3 anorexia in three patients (13.6%), grade 3 febrile neutropenia in three patients (13.6%) and grade 5 pneumonitis in two patients (9.1%). These patients died with respiratory failure induced by the progression of combined pulmonary fibrosis and emphysema. Further studies are required to evaluate the efficacy and toxicity of this regimen.

**A RETROSPECTIVE ANALYSIS OF CHEMOTHERAPY WITH S-1 AFTER THE STANDARD TREATMENT OF NON-SMALL-CELL LUNG CANCER**


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**Background:** All patients with advanced non-small cell lung cancer received disease progression after first-line chemotherapy. The median survival is between 4 and 5 months without second-line chemotherapy. There are currently three agents approved for treating patients who progress after one prior regimen: docetaxel, pemetrexed and erlotinib. Evidence of other treatment with drugs, including S-1 is unclear.

**Patients and methods:** All patients had adequate hematologic and biochemistry parameters with a good performance status and advanced non-small-cell lung cancer. They are already treated with guideline recommended chemotherapy regimens. From April 2010 through February 2012, five patients were received chemotherapy using S-1 and four with CBDCA + S-1. The disease control rate after 12 weeks was 89%, but there were no PR. The main toxicity was myelosuppression, gastrointestinal disorders. One case of grade 4 mucosal damage, one case of grade 3 diarrhea and one case of grade 3 thrombocytopenia were observed. Other adverse events were mild and could be tolerated.

**Conclusion:** Concerning patients with a good PS at the time of disease progression, chemotherapy using S-1 may be associated with a good disease control rate and an acceptable toxicity in spite of finishing guideline recommended chemotherapy. The prospective study for third- or fourth-line chemotherapy with S-1 should be considered.
**Results:** We identified 76 patients. DP/CV/CbP were enrolled in 25/44/7 patients. The median age was 68 years (37–74); male/female, 57/19; F/S 01/46, 33%; Ad/Sq/NO, 41/29/14; and clinical stage IIIB/III/IV, 4/32/40. Dose delivery of chemotherapy was 88/20/80% (DP/CV/CbP) and that of TRT was 93/92/99%. Sixty-three patients responded to the therapy, including five CR (2/3/0), 58 PR (19/3/4) and 11 SD (1/1/9). Forty-four patients had recurrence (12/27/5). Among them, 21 patients recurred at a local site (6/10/5) and 23 patients at a distant site (4/17/2). Of this, 45 patients developed grade 3 or greater hematological toxicities (10/33/2). Non-hematological toxicities were grade 3 radiation esophagitis in four patients (2/1/1) and grade 3 radiation pneumonitis in seven patients (2/3/2). A 69-year-old man who had received a right lower lobectomy for lung adenocarcinoma (pT1N0M0), recurred with brain metastasis 3 years later and treated with gamma-knife therapy, was referred to our hospital. CT showed a right hilar mass and enlarged mediastinal lymph nodes. An endoscopically visible tumor protruding into the lumen of the right upper lobe was biopsied. Histopathology revealed CD56+ and synaptophysin-positive neuroendocrine carcinoma. ALK protein expression was positive by IHC but ALK rearrangement was negative by FISH using a dual-color break-apart probe. Interestingly, positive immunostains of ALK, CD56 and synaptophysin were observed in primary lung adenocarcinoma but no ALK rearrangement was shown by FISH. The patient received chemotherapy with carboptin and pemetrexed. After local progression, he was treated with carboptin and etoposide.

**Conclusions:** A case of lung adenocarcinoma with neuroendocrine differentiation exhibiting discordance between IHC and FISH for ALK was presented. Although FISH is a gold-standard reference, sensitivity and specificity of IHC for ALK protein or the relationship between IHC and FISH for ALK should be further investigated in a large number of patients.
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Abstract: Purpose: In recent years, detection of EGFR mutation and its sensitivity to TKI were considered to be a predictive marker for side-effects of PEM. However, as it is not always easy to obtain both tumor tissue and blood from advanced cancer patients, we have developed a new strategy that can utilize multiple options for EGFR genetic analysis. The aim of this study was to evaluate the feasibility of PEM’s predictive markers by comparing the test system with those based on existing systems.

Background: There are a variety of methods for detecting EGFR mutations. Our present strategy can be applicable for deciding lung cancer treatment, which can be used in patients with advanced non-Sq NSCLC. Materials and methods: We retrospectively analyzed 20 PEM patients who were treated with PEM alone or PEM containing regimen. We retrospectively analyzed 20 PEM patients. We compared the test system with those based on existing systems (nucleic acid-locked nucleic acid PCR and LTR-PCR) and cycleave real-time PCR assay and fragment analysis. Results: We retrospectively analyzed 20 PEM patients. We compared the test system with those based on existing systems (nucleic acid-locked nucleic acid PCR and LTR-PCR) and cycleave real-time PCR assay and fragment analysis. Conclusion: We could confirm the usefulness of this strategy of this disease. However, the number of cancer cells obtained from a specimen is limited. Therefore, it is important to develop a new strategy for the estimation of the number of cancer cells in patients treated with PEM.

Poster Session 7: Lung cancer EGFR 1
P1-043 CIRCULATING TUMOR CELLS AND T790M IN METASTATIC NON-SMALL-CELL LUNG CANCER PATIENTS WITH EGFR MUTATIONS AND ACQUIRED RESISTANCE TO TKI
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Abstract: Purpose: The study assessed correlations between the presence of circulating tumor cells (CTCs), detection of T790M in organs with metastases or circulating-free DNA (cfDNA), and prognosis in metastatic NSCLC patients with acquired resistance to EGFR-TKI. Materials and methods: Twenty NSCLC patients with activating EGFR mutations, who initially responded but subsequently experienced disease progression while on EGFR-TKI treatment, were defined as having acquired resistance. Blood samples were collected after the development of such acquired resistance and CTCs were counted using the CellSearch system (Veridex). At the same time, T790M in acquired resistant or cfDNA was analyzed by cycling real-time PCR assay and fragment analysis.
Results: Six men and 14 women with a mean age of 63.5 years (22-84) were enrolled. Histological subtypes were adenocarcinoma in 19 and squamous cell carcinoma in the remaining one. Clinical stages were stage IV in 14 and recurrence with distant metastases after distant resection in 6. EGFR mutations in tumors at the primary site were G719C in 1, exon 19 deletion in 7, L858R in 10 and G791C + L858R in 2. CTCs were detected in eight (40%). Numbers of CTCs (per 7.5 ml blood) were 1 in four cases and 3, 4, 8 and 24 in one case each. Patients without CTCs survived significantly longer than those with CTCs (more than 1 per 7.5 ml). The mean survival time from the first detection of CTCs was 3.0 months in patients with CTCs and not reached in patients without CTCs (P = 0.001). T790M was detected in six cases (30%). T790M was found in 75% (n = 6/8) of patients without CTCs but in 0% (n = 0/2) of those with CTCs (P = 0.001).
Conclusions: The presence of CTCs was correlated with poorly prognosis and lack of T790M in acquired resistant or cfDNA. The presence of CTCs was informative for distinguishing patients with or without T790M.
patients were treated with PEM as the cytotoxic agent second-line setting. Four patients were with PEM + BEV. Six of 13 patients who received the PEM–platinum combination chemotherapy as the cytotoxic agent first-line setting achieved the objective response and the overall response rate (ORR) was 46%. Prior treatment-free survival (PFS) was 4.2 months in this population. In the other hands, none of 10 patients who received the PEM alone as the cytotoxic agent second-line setting achieved the objective response and ORR was 0%. PFS was 1.6 months.

Conclusions: The PEM-platinum regimen is effective for the EGFR-mt NSCLC in the cytotoxic agent first-line setting. However, PEM alone might not be active for the EGFR-mt NSCLC in the cytotoxic agent second-line setting.

Poster Session 8: Lung cancer EGFR 2

P1 – 095

COEXISTENCE OF POSITIVE MET FISH STATUS WITH EGFR MUTATIONS SIGNIFICANTLY POOR PROGNOSIS IN PRIMARY LUNG ADENOCARCINOMA

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Overexpression of MET has been reported in various malignancies and is associated with cell proliferation, inhibition of apoptosis and metastasis. MET amplification has been reported to contribute to acquired resistance to epidermal growth factor tyrosine kinase inhibitors (EGFR-TKI) in non-small-cell lung cancer (NSCLC), being observed among 5–10% of those patients. Therefore, MET gene alterations could be both prognostic and predictive, and evaluation of that is indispensable in practice. However, the frequency of positive cases varies due to a lack of standardized criteria of fluorescence in situ hybridization (FISH). The purpose of this study is to find which criteria could be useful in terms of the association with clinical characteristics. We evaluated the MET gene copy number of FISH using two different criteria in lung adenocarcinoma: the Cappuzzo scoring system and PathVysion and its association with clinicopathological characteristics. MET positive cases according to the Cappuzzo scoring system evidenced both aneuploidy and true amplification, whereas PathVysion revealed only amplification. One hundred and thirty-eight lung adenocarcinoma tissue samples were evaluated, and the proportion of MET FISH positive cases was 15 and 4% determined by the Cappuzzo system and PathVysion, respectively. PathVysion demonstrated higher frequencies of MET FISH positives among men and smokers and evidenced no MET FISH positives in patients with bronchiolovascular tumors. Prognosis was significantly associated with MET FISH positive only as defined by the PathVysion system (gene amplification), not by the Cappuzzo system. However, the progression-free survival time of patients with both EGFR mutations and MET FISH positive defined by the Cappuzzo scoring system was significantly shorter than with EGFR mutations alone. These results suggest that MET FISH is a potential prognostic factor and co-existence of MET FISH with EGFR mutations signifies worse prognosis.

Results:

Conclusions: Our result showed homogeneity of EGFR mutation within the resected adenocarcinoma of lung. Even fine needle aspiration can extract the representative tumor cells for EGFR mutation detection. However, in the metastatic lung cancer, differential rate (ORR) was 46%. Prior treatment-free survival differed. Hence, the result of the EGFR mutation assay depends on where the biopsy is taken.

Poster Session 8: Lung cancer EGFR 2

P1 – 059

WHAT FACTORS AFFECT LONG-TERM SURVIVAL AFTER RESPONDING TO GEFITINIB IN ADVANCED NON-SMALL-CELL LUNG CANCER? REAL WORLD EVIDENCE

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Background: After gefitinib was approved in July 2002, we experience long-term survival patients in the actual clinical setting. However, it is not clear how the factors or treatment strategy are contributing to the long-term surviving patients. We evaluated the effects of clinical backgrounds and treatment histories on overall survival (OS).

Methods: We extracted information on advanced NSCLC patients with the following inclusion criteria from the medical records: (i) patients who were diagnosed by October 2010 and treated with gefitinib after July 2002; (ii) performance status (PS) 0–2; (iii) FF, CR or OR on long SD (6 months or more) by gefitinib treatment; (iv) patients who had not received curative surgical operation or curative radiation therapy. The primary objective is to evaluate the survival time of the patients who responded to gefitinib and clarify the relationship between clinical factors and survival time. We also conducted Dynamic Treatment Regimen Analysis (DTRA) to explore the key treatment regimens and the sequence of regimens contributing to long-term survival.

Results: The medical records of total of 275 patients were extracted; 44% (122/275) were EGFR mutation examined and 93% (114/122) has shown the EGFR mutation positive. The mean age was 65, 72% (198/275) were women, 66% (182/275) were non-smokers and 90% (247/275) had adenocarcinoma histology. 30% (54/275) had adenocarcinoma histology. 20% (54/275) and 21% (58/275) were with PEM + BEV. Six of 13 patients who received the PEM backbone alone. PEM alone might not be active for the EGFR-mt NSCLC in the cytotoxic agent first-line setting achieved the objective response rate (ORR) was 0%. PFS was 1.6 months.

Conclusions: This study suggests that sex and gefitinib re-administration may have significant effects on OS in long survivors after responding gefitinib treatment.

Poster Session 8: Lung cancer EGFR 2

P1 – 056

CYTOKERATIN 19 FRAGMENT (CYFRA21-1) PREDICTS THE EFFICACY OF THE EPIDERMAL GROWTH FACTOR RECEPTOR TYROSINE KINASE INHIBITOR (EGFR-TKI) IN NON-SMALL-CELL LUNG CANCER (NSCLC) HARBORING EGFR MUTATION

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Background: EGFR mutation is independently associated with a favorable response in NSCLC patients receiving EGFR-TKIs, regardless of gender or smoking history. However, recent reports have indicated that squamous cell carcinoma patients harboring EGFR mutations show a worse response to EGFR-TKIs than adenocarcinoma patients. We hypothesized that serum CYFRA21-1 is a predictive marker in EGFR-mutated patients treated with EGFR-TKIs.

Methods: We retrospectively screened 160 NSCLC patients harboring EGFR mutations (exon 19 deletions, L858R in exon 21, or other minor mutations) who received either gefitinib or erlotinib between 1992 and 2011. Patients were screened for histology, sex, age, smoking status, efficacy of EGFR-TKI and tumor markers (CEA/CYFRA21-1) at initial diagnosis.

Results: Out of 160 eligible patients treated with EGFR-TKIs, 77 patients with a high CYFRA21-1 level (>2 ng/ml) showed statistically shorter progression-free survival (PFS) than 83 patients with a normal CYFRA21-1 level (median PFS 7.5 versus 14.0 months, P = 0.006). No significant difference in PFS was observed between the high CEA group (>5 ng/ml) and the normal CEA group (median PFS 8.6 versus 11.2 months, P = 0.3423). Multivariate analysis revealed that a high CYFRA21-1 level is independently associated with PFS (HR 1.35; P = 0.003) as well as squamous cell carcinoma (HR 1.40; P = 0.020) and performance status 2 (HR 2.63; P = 0.001).

Conclusions: CYFRA21-1 seems to be a reliable marker in NSCLC patients harboring EGFR mutations.
Poster Session 9: Gastrointestinal cancer case 1

P1 - 059

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A 61-year-old woman complaining of anorexia and general fatigue admitted to our hospital for further examination. She was examined and diagnosed as advanced sigmoid colon cancer with multiple metastases of the lung, liver and left hydronephronphrosis. Since curative surgery was deemed not possible, we started chemotherapy with bevacizumab + FOLOFOX (biphasically drip infusion). After the sixth course, colonoconscopy revealed a significant tumor reduction and changes to scar tissues. CT did not reveal complete disappearance but some reduction in metastases of the lung and liver. Sigmoidection and lymph node resection (D1) were carried out. We did not disapper any dissemination and the histological diagnosis revealed complete disappearance of cancer cells in the main tumor. She was discharged 13 days after the surgery following the chemotherapy including bevacizumab and XELOX. The chemotherapy using bevacizumab + FOLOFOX was a candidate for the standard treatment strategy for advanced colon cancer inoperable. Herein, we report this rare case with a view of the literature.

Poster Session 11: Gastrointestinal cancer/esophageal cancer 1

P1 - 075

Efficacy and Safety of Chemoradiotherapy for Patients with Locoregional Lymph Node Recurrence of Esophageal Squamous Cell Carcinoma


Background: Although no standard treatment has been established for recurrent esophageal cancer, several studies have suggested the efficacy of chemoradiotherapy (CRT) for the locoregional lymph node recurrence of esophageal squamous cell carcinoma (ESCC).

Objective: The aim of this study is to evaluate the efficacy and safety of CRT for patients with the locoregional lymph node recurrence of ESCC.

Methods: Between 2002 and 2009, 167 consecutive patients with thoracic ESCC underwent curative esophagectomy at Shizuoka Cancer Center; of these patients, 41 were diagnosed as locoregional lymph node recurrence. We retrospectively reviewed the data of 30 patients who satisfied the following selection criteria: (i) PS 0–1; (ii) adequate organ function; (iii) no previous radiotherapy (RT) and (iv) concurrent CRT by split regimen (two courses of 5-FU 400 mg/m2 on days 2/4; adjuvant chemotherapy (+/- CDDP 70 mg/m2 on day 1, 4 weeks for one cycle) and chemotherapy including bevacizumab and XELOX. The chemotherapy using bevacizumab + FOLOFOX was a candidate for the standard treatment strategy for advanced colon cancer inoperable. Herein, we report this rare case with a view of the literature.

Results: The characteristics of the 30 patients were as follows: median age, 65 years (range: 44–77); men/women, 29/1; PS (0/1), 20/10; primary tumor location (upper/middle/lower), 4/19/7; stage (I/IIA/IIIB/IIV), 1/15/17/2; adjuvant chemotherapy (+/-), 20/10; site of recurrence (cervical/mediastinal/ abdominal/other), 6/20/5; number of recurrent lymph nodes (1/2 >), 18/12. The median time to recurrence from surgery is 11 months (range: 3–57) and 28 patients (93%) completed the planned CRT regimen. The median follow-up period is 25.5 months (range: 66.7–7). The complete response rate was 56.7%. The median PFS and the median OS were 9.1 and 22.3 months, respectively. The frequency of grade 3/4 adverse events (CTCAE ver4.0) as follows: leukopenia (30%), neutropenia (23%), anemia (13%), appetite loss (17%) and nausea (7%). No treatment-related deaths occurred.

Conclusion: CRT is an effective and safe treatment option for the locoregional lymph node recurrence of ESCC.

P1 - 081

The Clinical Benefit of Chemoradiotherapy for Recurrent Esophageal Cancer

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Objective: The standard therapy for recurrent esophageal cancer is systemic chemotherapy. However, in cases in which the recurrent lesion is confined to the area where radiotherapy is applied, chemoradiotherapy will be able to provide better local control and prognosis.

Method: A retrospective study was carried out on 14 patients with local recurrent esophageal cancer but no other metastasis who underwent chemoradiotherapy (FP+RT: 5FU 700 mg/m2/day on days 1–4, CDDP 70 mg/m2 on day 1, 4 weeks for one course x 2, RT: 66–66 Gy [30–33 Fr] at Toyama Prefectural Central Hospital between April 2008 and February 2012)

Results: The subjects included 13 men and 1 woman. The median age was 64 years (PS0/1/2 = 3/9/2). The histology was classified into squamous cell carcinoma in 13 subjects and carcinosarcoma in one subject. The site of the radiation therapy was recurrence in the lymph nodes in 10 patients, anastomotic recurrence in 3 patients and recurrence in pleural nodes in 1 patient. Regarding the tumor reduction effect, the lesions of 12 patients were evaluable by RECIST, and the response rate was 66.6%. The median of progression-free survival (PFS) was 251 days (8.4 months) and the median of overall survival was 475 days (15.8 months). Exacerbation of the irradiated lesions was observed in four patients (31%), whereas new lesions at other sites were observed in seven patients (55%). G3 or more adverse events were hematologic toxicity (23%) and non-hematologic toxicity (23%), such as anorexia and nausea.

Discussion and conclusion: This study showed that chemoradiotherapy for local recurrent esophageal cancer provides the excellent local control. The severity of adverse reactions caused by the therapy was relatively mild, and OS was good. In the future, the relationship between transient local control and survival time should be studied in a prospective setting.
P1 – 082

TREATMENT RESULTS OF DEFINITIVE CHEMORADIOGRAPHY WITH ELECTIVE NODAL IRRADIATION FOR PATIENTS WITH CLINICAL STAGE I (T1B) ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Background: Surgical studies reported that ~30% of patients with a clinical stage (c-stage) I esophageal squamous cell cancer (ESCC) had evidence of occult metastases on lymph node dissection. Involved field radiotherapy (IFRT) raises concern over potentially increased nodal treatment relapse. In JCOG 9708 (a phase II trial of definitive CRT with IFRT for c-stage I ESCC), 8/72 (11.1%) patients experienced lymph node relapse, and 4-year overall survival rates were 80.5%. Elective nodal irradiation (ENI) delivers prophylactic radiation to clinically uninvolved lymph nodes. There are few reports on CRT in combination with ENI, and this retrospective analysis evaluated the treatment results for patients treated with ENI for a c-stage I (T1b) ESCC.

Methods: Between July 2004 and April 2009, 54 patients with c-stage I (T1b) thoracic ESCC were treated with definitive CRT in our institution. Of these 54 patients, 33 were selected after applying the following inclusion criteria: (i) age between 20 and 75 years; (ii) radiotherapy was applied with multifield irradiation including ENI; (iii) radiation dose was 50.4 Gy over 28 fractions as 1.8 Gy per fraction; (iv) treatment consisted of cisplatin 70 mg/m² on days 1 and 35 and 5FU 700 mg/m² from 1–6; (v) no prior chemotherapy or radiotherapy; and (vi) adequate function of major organs.

Results: The median age was 66 and all patients had an ECOG PS of 0 or 1. The median follow-up period was 57 months. There were 28 complete remissions (88%). Four-year overall and progression-free survival rates were 80% and 62%, respectively. Treatment relapse was observed in five patients. The first site of failure was the primary lesion in four patients, and regional lymph nodes in-field in one case, and there were no distant metastases. Grade 3/4 leukopenia, thrombocytopenia, anorexia and nausea were observed in 14 (42%), 4 (12%), 3 (9%) and 2 (6%) patients, respectively. Grade 3 interstitial pneumonia as a late toxic effect occurred in one patient (3%). There was no treatment-related death.

Conclusion: CRT with ENI for patients with c-stage I (T1b) ESCC was tolerable, and (vi) adequate function of major organs.

Poster Session 12: Gastrointestinal cancer esophageal cancer 2

P1 – 086

5-FU INDUCED ENCEPHALOPATHY DURING 5-FU CONTAINING REGIMEN FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Background: 5-FU-induced encephalopathy was known as an uncommon toxicity during the treatment which contain with 5-FU. But there were few reports such as a clinical feature and risk factors of 5-FU-induced encephalopathy. We conducted a retrospective case-control study to investigate the clinical feature and risk factor of them.

Methods: Data were collected from the medical record. The selection criteria were as follows: pathologically proven esophageal squamous cell carcinoma, patients who received 5-FU containing regimen in our hospital. The diagnostic criteria of the 5-FU induced encephalopathy includes: (i) development of encephalopathy during or shortly after the completion of 5-FU administration; (ii) exclusion of other metabolic factors that may affect consciousness and (iii) exclusion of an adverse effect by concomitant medications. 5-FU containing regimens include that 5-FU + CDDP with or without radiation, 5-FU + nedaplatin with or without radiation and 5-FU + CDDP + APR.

Results: From January 2008 to March 2010, 317 patients were collected. Of 317 patients, the median age was 64 (range 36–79); male/female, 267/49, cStage I/I/II/III/IV, 63/19/53/91/85. The median and the total course of 5-FU containing regimen were 2 (range 1–4) and 943. The object of first treatment was as follows: nonradiotherapy in 114, definitive chemoradiotherapy in 110, palliative chemotherapy (n = 81) and others (N = 24). Nine patients (2.8%) were diagnosed as 5-FU encephalopathy. The median course and time to onset of encephalopathy was 3 course (range 1–4) and 5 days (range 3–6) from the start of 5-FU. Five of six patients who examined NH3 were observed the elevation of NH3. Head CT or MRI showed no abnormality in all patients. Univariate analysis showed that only age (>60) was the risk factor (P = 0.034). The creatinine level at days 4–6 during chemotherapy more elevated in the encephalopathy group (P = 0.004), and the Na level at days 4–6 were more decreased in the encephalopathy group (P < 0.001).

Conclusion: 5-FU encephalopathy was rare but more frequently occurred in aged patients. Transient change of creatinine and Na may be significance to the mechanisms of 5-FU encephalopathy.
Conclusion: of the hands before the treatment was 4.3, which decreased to 4.1 after 4 weeks and was 88.9%. According to the NRS analysis of the completion cases, the median value as 2 of 29 registered cases did not satisfy the evaluation criteria, they were conducted so that the detailed improvement of the dysfunction symptoms and neural daily. The hands and feet were studied, respectively, to evaluate by the numerical thus, it is considered to be effective to be used at clinical practice.

Methods: We investigated serum levels of Na in 67 breast cancer patients who received CPA-combined therapy with the use of AP or not. They all received 600 mg/m² of CPA combined with either of doxorubicin, epirubicin, or docetaxel. Their prior electrolytes were to be within the normal range. In the first cycle, we evaluated serum Na levels before the CPA start and those of 24 h after. We defined a serum Na level lower than 135 mEq/l as ‘hyponatremia’.

Results: The background between the two groups, with AP and without AP, was comparable, in whom the prior Na levels were 140.0 ± 1.97 and 140.1 ± 1.88 mEq/l, in the AP group and in the non-AP group, respectively. The chemotherapies including CPA, the clinical stages, the uses of serotonin-receptor antagonist and dexamethasone were comparable between the two groups. Hyponatremia occurred in 11 of 42 (26.2%) patients in the AP group, whereas 2 of 25 patients (8.0%) in the non-AP group. Since the rate in the non-AP group was comparable with the previous reports, hyponetremia seemed to occur frequently in the AP group. The average Na level at 24 h after chemotherapy was 136.49 ± 3.94 mEq/l in the AP group and 138.68 ± 3.05 mEq/l in the non-AP group, respectively. Among 11 patients who developed hyponatremia, they were resolved within 48 h without any treatments in 10 patients and only one needed the Na replacement. The patient did not develop hyponatremia without using AP in the third cycle.

Conclusions: According to our cohort study, AP might frequently cause hyponatremia in the CPA-combined chemotherapy.

Poster Session 15: Palliative and supportive care neuropathy

PHASE II STUDY MENTHOL FOR CANCER CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY

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Purpose: Cancer chemotherapy induced peripheral neuropathy not only significantly decreases the patients QOL but can also affect the therapeutic efficacy. Menthol is TRPM-8 agonist and is reported to have indicated some effects on neuropathic pain. TRPM-8 agonist and is reported to have indicated some effects on neuropathic pain.

Method: 1.35% menthol ointment was given to the subjects, who applied it twice a day. Although we have experienced several cases of severe hyponatremia probably caused by AP. Therefore, the evaluation was conducted so that the detailed improvement of the dysfunction symptoms and neural symptoms could be evaluated.

Results: As of 2 of 29 registered cases did not satisfy the evaluation criteria, they were excluded. Therefore, 27 cases were studied for the evaluation. The compliance rate was 88.9%. According to the NRS analysis of the completion cases, the median value of the hands before the treatment was 4.3, which decreased to 4.1 after 4 weeks and to 3.6 after 8 weeks. As to the feet, the median value before the treatment was 5.4, which decreased to 4.9 after 4 weeks and to 4.4 after 8 weeks. Although the evaluation using PNS indicated one or more decrease in 19 of 24 cases, 5 of 24 cases indicated no improvement by either NRS or PNS.

Conclusion: As a result of this experiment, the improvement ratio was 75%, which led to the conclusion that menthol is effective for peripheral neuropathic pain as supportive care. The discontinuation ratio due to adverse effects is as low as 11%, which were quickly improved upon discontinuation and the safety was confirmed; thus, it is considered to be effective to be used at clinical practice.

Poster Session 17: Urologic cancer 1

PROGNOSTIC FACTORS OF RENAL COLLECTING DUCT CARCINOMA BASED ON CLINICAL FEATURES AND EFFECTIVE CHEMOTHERAPY

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Background: Collecting duct carcinoma (CDC) of the kidney is an aggressive disease with a poor prognosis and accounts for less than 1% of all renal cancers. To date, there is still no established standard therapy for CDC. The aim of this study is an investigation of clinico-pathologic findings of CDC and the correlation of disease status with a prognosis. Methods: From 1996 to 2009, 35 patients with CDC were treated at eight medical centers. The diagnosis of CDC was made based on nephrectomy in 27 cases and renal biopsy in 8 cases. We report on tumor characteristics, patient treatments and outcomes.

Results: The median age was 56 years (range, 29–82 years). Twenty seven of the 35 patients underwent nephrectomy for initial treatment, 4 patients received chemotherapy, and 4 patients did not receive any treatment. The median follow-up was 15.8 months (range, 0.6–88.4 months). Fourteen (40%) deaths were reported. The median progression free survival (PFS) and overall survival (OS) were 5.47 months (95% CI 3.97 to 6.96) and 45.37 months (95% CI 0.10 to 19.2), respectively. Of the 35 patients, 21 patients received chemotherapy (4 with Gemcitabine/platinum, 3 with Methotrexate, Vinblastine, Adriamycin, and Cisplatin, immunotherapy (10 with IFN ± IL-2), and targeted therapy (4 with Sunitinib). Median time to progression (TTP) for the treated patients was 2.9 months, with no statistically significant difference between the therapies (P=0.853). The median OS (overall survival) for patients for stage IV who had a palliative chemotherapy was 18.40 months (95% CI 0 to 41.94) and the median OS for those who did not was 45.33 months (95% CI 0 to 9.12). This showed that those who were treated had a significantly better OS rate (p=0.018).

Conclusions: CDC is a highly aggressive form of renal cell carcinoma. Most of all, accurate diagnosis is the most important for appropriate treatment. Although surgical treatment is the mainstay of the treatment, it is rarely possible to cure CDC completely with surgery alone. Thus, the study about the necessity and age role of adjuvant treatment after surgery is needed. So far, the treatment of these
patients has been based on a number of chemotherapy regimens, including cisplatin–gemcitabine and immunotherapy because the distal nephron is the origin that makes this tumor more similar to urothelial carcinoma. The results of these experiences, however, have been somewhat disappointing. So, further studies might be needed to identify the role of targeted agents and to develop them based on biology.

**P1 – 122**

**MAMMALIAN TARGET OF RAPAMYCIN INHIBITORS VERSUS VASCULAR ENDOTHELIAL GROWTH FACTOR TYROSINE KINASE INHIBITORS (VEGF TKI) AS SECOND- LINE THERAPY IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA AFTER FAILURE OF FIRST- LINE VEGF TKI: SINGLE CENTER RETROSPECTIVE ANALYSIS**

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**Background:** Sequential therapy is a standard strategy used to overcome the limitations of targeted agents in metastatic renal cell carcinoma. It remains unclear whether a mammalian target of rapamycin (mTOR) inhibitor is a more effective second-line therapy after first-line VEGF TKI has failed than the alternative, vascular endothelial growth factor tyrosine kinase inhibitor (VEGF TKI).

**Methods:** A clinical database was used to identify all patients with mRCC treated with VEGF TKIs in the Asan Medical Center. Medical records were reviewed to identify those patients in whom first-line VEGF TKI failed and who were then treated with second-line VEGF TKI or mTOR inhibitors. Patient medical characteristics, radiological response and survival status were assessed.

**Results:** Of the 83 patients who met the inclusion criteria, 41 received second-line VEGF TKI (sunitinib (n = 16) and sorafenib (n = 25)) and 42 were treated with mTOR inhibitors (temsirolimus (n = 11) and everolimus (n = 31)). After a median follow-up duration of 23.9 months (95% CI: 17.8–30.0), progression-free survival was 3.0 months for both groups (hazard rate (HR), VEGF TKI versus mTOR inhibitor) = 0.97, 95% CI: 0.59–1.62, P = 0.92). Overall survival was 10.6 months for the VEGF TKI group and 8.2 months for the mTOR inhibitor group (HR = 0.98, 95% CI: 0.57–1.68, P = 0.94). The two groups did not differ significantly in terms of the disease control rate (51% for VEGF TKI and 59% for mTOR inhibitor, P = 0.75).

**Conclusions:** Second-line VEGF TKI seems to be as effective as mTOR inhibitors and may be a viable option as a second-line agent after first-line anti-VEGF agents have failed.

**P1 – 123**

**EFFICACY AND SAFETY OF SUNITINIB IN PATIENTS WITH NON-CLEAR CELL RENAL CELL CARCINOMA**

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**Background:** Retrospective and molecular biological data suggest that sunitinib may be effective in patients with non-clear cell renal cell carcinoma (nccRCC).

**Methods:** Eligibility criteria included advanced nccRCC except for collecting duct carcinoma and sarcomatoid carcinoma without identifiable renal cell carcinoma subtypes. Patients were treated with 50 mg/day oral sunitinib for 4 weeks, followed by 2 weeks of rest. The primary end point was the overall response rate.

**Results:** Thirty-one eligible patients were enrolled. Twenty-four patients (77%) had prior nephrectomy. By Memorial Sloan-Kettering Cancer Center criteria, 8 patients (26%) had poor risk and 14 (45%) had intermediate risk. Twenty-two patients had papillary RCC, and 3 had chromophobe RCC. Eleven patients had partial response, with a response rate of 36% (95% CI, 19–52%) and an additional 17 patients (55%) had stable disease. The median duration of response was 12.7 months (95% CI: 6.3–19.1 months), and the median progression-free survival was 6.4 months (95% CI: 4.2–8.6 months). At a median follow-up duration of 18.7 months (95% CI: 13.7–23.7 months), 13 patients (42%) had died, resulting in an estimated median survival of 25.6 months (95% CI: 8.4–42.9 months). Tumor toxicity profiles were commensurate with prior reports.

**Conclusions:** Sunitinib has promising activity in patients with nccRCC. (NCT01219751) Final survival results will be reported in the meeting.

**P1 – 124**

**CLINICAL FEATURES IN RENAL CELL CANCER PATIENTS IN TKI ERA: AN ANALYSIS OF WEB-BASED REGISTRY DATA, KOREA CANCER STUDY GROUP, GU & GY COMMITTEE, KCGS GU10-12**

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**Background:** Korean Cancer Study Group, GU & GY cancer committee carried out a multicenter web-based registry of renal cell cancer patients' clinical data. The aim of this RCC registry study is to investigate clinicopathologic findings of Korean renal cell cancer patients associated with diagnosis, treatment behavior and its outcomes.

**Methods:** A total of 979 patients from 14 hospitals were registered. The patients of the participating hospitals who were diagnosed as RCC between the years 2007 and 2011 were registered.

**Results:** The median age at diagnosis was 59 years and the male/female ratio was 2.35. The most common presenting symptoms and sign was pain associated palpable mass and hematuria was common. The major pathologic subtype of RCC was the clear cell type (82.1%). Other subtypes were papillary cell type (6.1%), chromophobe type (5.9%), unclassifiable type (4.1%) and others. According to Fuhrman grading system, grade 1 was 10.8%, grade 2 24.1%, grade 3 37.6% and grade 4 7.5%. Both the kidney were equally involved and bilateral involved case was nine cases. According to the TNM stage, stage I patients was 60.6%, stage II 10.6%, stage III 9.8% and stage IV 18.9%. In advanced metastatic RCC patients, the lung, bone, liver and distant lymph node were common metastatic sites. Surgical excision including metastectomy and cytoreductive surgery was carried out in 90.2% of all patients. Anticancer immunotherapy or chemotherapy was done in 6.7%, chemotherapy with oral TKI or mTOR inhibitor in 60.7% and supportive care in 32.7%. The objective response rate of first-line palliative chemo- and/or immunotherapy among metastatic RCC patients including systemic relapsed patients was 7.5%. And the disease control rate including stable disease was 49.3%. The median overall survival in metastatic RCC patients was 19.2 months.

**Conclusions:** We demonstrate baseline disease characteristics as well as clinical features of renal cell cancer patients from multihospital in Korea. These data were collected from web-based registry of Korea RCC patients and analyzed using the web-based data system.

**P1 – 125**

**PRIMARY URETHRAL CANCER: A RETROSPECTIVE ANALYSIS OF 27 PATIENTS AT A SINGLE INSTITUTE**

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**Background:** There is a paucity of information in the literature on primary urethral cancer (PUC). We carried out a retrospective study regarding the treatment and outcome in patients (pts) with PUC.

**Methods:** Twenty-seven consecutive pts (3 males and 24 females) with a confirmed diagnosis of PUC undergoing initial treatment between 1997 and 2011 at Asan Medical Center in Korea were reviewed. Low stage was defined as T2N0M0 or less and high stage was defined as more advanced stages.

**Results:** The median age was 57 years (14–83). Thirteen pts had low stage and 14 pts high stage. In the low-stage group (n = 13), 10 pts underwent surgery and 3 pts received chemoradiotherapy. A surgical complete resection (R0) achieved in 90% (9/10) and one patient with microscopically positive resection (R1) was treated with post-operative radiotherapy. Two (15.4%) pts in the low-stage groups had local recurrence with local failure. In the high-stage group (n = 14), 11 pts underwent radical resection, 2 pts received chemoradiotherapy and 1 patient with distant
metastasis received chemoradiotherapy. R0 achieved in 45.5% (5/11) and 6 pts with R1 were treated with post-operative radiotherapy (n = 4), chemoradiotherapy (n = 1) or chemotherapy (n = 1). In the high-stage group, there was no difference in survival outcomes between R0 (n = 5) and R1 (n = 6), and seven pts with recurrence after surgery had six distant metastasis and one local failure. The remaining two pts treated with chemoradiotherapy in the high-stage group showed the event-free survival of 42 and 53 months, respectively. With a median follow-up of 40 months (1–158), low stage was associated better event-free survival and overall survival compared with high stage (log-rank test: P = 0.006 and P = 0.002, respectively).

Conclusions: High-stage PUC showed different clinical behaviors and managements compared with low stage. In this study, surgery is pivotal in PUC pts with low stage. The multidisciplinary approach may be required to obtain an optimum oncologic outcome in high-stage PUC.

Poster Session 18: Urologic cancer 2

P1 – 128
PALONOSTRON WITH APREPITANT–Dexamethasone TO PREVENT CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING DURING GEMCITABINE/CISPLATIN IN UROTHELIAL CANCER PATIENTS

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Background: The combination of gemcitabine and cisplatin (GC) is a standard regimen for advanced urothelial cancer (UC). Although this is a high emetogenic chemotherapy, there has been no study concerning antiemetic prophylaxis for chemotherapy-induced nausea and vomiting (CINV) during GC. The aims of this study were to evaluate CINV during GC and to compare the antiemetic efficacy of the triple combination of palonosetron, aprepitant and dexamethasone with that of our old regimen using ondansetron and dexamethasone.

Methods: We conducted a retrospective review of the medical records of 52 patients who received GC for advanced urothelial cancer between February 2005 and January 2012. Uncontrolled CINV events were identified through records of nausea and vomiting, additional infusion, rescue medications and/or records of food intake. Nausea, vomiting and anorexia were classified using the Common Terminology Criteria for Adverse Events (CTCAE) ver4.0.

Results: A total of 23 and 29 patients were treated with ondansetron–dexamethasone (group 1) and palonosetron with dexamethasone–aprepitant (group 2), respectively. There was no significant difference in age, gender or the dose of cisplatin between the two groups. Patients in group 2 were more likely to achieve more favorable CINV control, e.g. a lower grade of nausea, vomiting or anorexia, lower incidence of rescue therapy required and shorter time to become CINV-free, than patients in group 1.

Conclusions: This study shows that palonosetron in combination with aprepitant and dexamethasone is more effective to prevent chemotherapy-induced nausea and vomiting during GC and to compare the antiemetic efficacy of the triple combination of palonosetron, aprepitant and dexamethasone with that of our old regimen using ondansetron and dexamethasone.

P1 – 127
REPEAT BIOPSY OUTCOMES AND CHANGE IN QOL STATUS AT 1 YEAR AFTER ACTIVE SURVEILLANCE: RESULTS FROM A JAPANESE MULTICENTER PROSPECTIVE STUDY AND THE PRIAS-JAPAN

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Backgrounds and objectives: In Japan, two prospective multicenter active surveillance (AS) studies are under investigation. The first is a prospective Japanese AS study that has been carried out in favorable risk prostate cancer since 2002. The second is the PRIAS-JAPAN; 30 institutions in Japan have been participating into the Prostate cancer Research International: Active Surveillance (PRIAS) study as the PRIAS-JAPAN since 2010. The objective of this study is to evaluate the outcomes of 1 year after AS including prostate re-biopsy and the change in QOL status using the two Japanese prospective cohorts.

Patients and methods: Thirteen institutions participated in the Japanese AS study. One hundred and thirty-four patients with biopsy proven favorable risk prostate cancer were enrolled into study between January 2002 and December 2003. AS remaining rate in 33.2%. On the other hand, the PRIAS-JAPAN study was started since January 2010. Until December 2011, 189 patients were enrolled. One year after rebiopsy was recommended to all participants, and QOL was assessed at enrollment and at 1 year after AS in both studies.

Results: In the Japanese AS study, 64 patients who underwent re-biopsy, 42 met the pathological selection criteria again. The reclassification rate was 34.4%. In PRIAS-JAPAN, the reclassification rate was 28% (P = 0.467). There was no predictive parameter for reclassification in the Japanese AS study. On the other hand, number of positive cores was a significant predictive parameter for reclassification in PRIAS-Japan. Almost all domains of QOL at enrollment revealed better QOL than norm-based scoring (NBS). At 1 year after AS, there was no significant change.

Conclusions: Instead of the time difference between the two studies was ~10 years, the reclassification rate for the current AS cohort (PRIAS-I) was comparable or even lower than the former cohort. Health-related QOL of the Japanese patients who opted AS as an initial treatment was better than NBS and it has been maintained 1 year after AS.

P1 – 129
ONCOLOGICAL OUTCOMES OF METASTATIC RENAL CELL CARCINOMA (mRCC) WITH MOLECULAR-TARGETED THERAPY IN ASAHIKAWA MEDICAL UNIVERSITY HOSPITAL

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Background: Since 2008, molecular-targeted therapy has been the standard systemic treatment of mRCC instead of IFN and IL-2. We have been accumulating our experience of molecular-targeted therapy for mRCC to analyze oncological outcomes. Herein, we present short-term outcomes of mRCC that was treated with molecular-targeted therapy in our institution.

Patients and methods: We retrospectively investigated oncological outcomes of 36 patients with mRCC who were treated with molecular-targeted therapy with or without nephrectomy.

Results: The median age was 66 years. Twenty-seven patients (75%) underwent nephrectomy and other 9 patients did not. Of the 27 patients who underwent nephrectomy, 24 (89%) received molecular-targeted therapy under adjuvant or salvage setting, whereas the other 3 patients received presurgical setting. The pathological type was clear cell carcinoma in 17 patients, non-clear cell in 9 and mixed type histology in 5. The remaining five patients did not undergo primary or metastatic site biopsy. The 2- and 3-year overall survival was 53.8 and 33.6%, respectively, from initial molecular targeted therapy. All nine patients without nephrectomy died within median time of 4 months. Thirteen patients had been treated with systemic therapy with IFN or IL-2 immunotherapy before initiation of molecular-targeted therapy. Twelve patients were treated with sequential therapy, including six cases treated with sorafenib, then sunitinib, followed by everolimus, five cases treated with sorafenib followed by sunitinib or vice versa and one case treated with sunitinib followed by temsirolimus. The most common grade 3 adverse events (AEs) were fatigue (18%) and hand-foot syndrome (12%). These AEs were manageable and reversible.

Conclusions: Our experience of molecular-targeted therapy for mRCC shows favorable oncological outcomes with acceptable tolerability. Molecular-targeted therapy cannot cure mRCC but probably can prolong patient survival without compromising their quality of life.
cancer. Our findings suggest the timing of perioperative chemotherapy is less important than whether or not a patient receives perioperative chemotherapy.

Poster Session 22: Malignant lymphoma

**P1 – 153** PROGNOSTIC IMPACT OF TUMOR-INFILTRATING FOXP3+ REGULATORY T CELLS IN DLBCL TREATED WITH R-CHOP

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**Background:** Tumor-infiltrating immune cells perform important functions in host immune response against diffuse large B cell lymphoma (DLBCL). We assessed the distribution and prognostic significance of FOXP3+ regulatory T-cells (Treg) in DLBCL.

**Patients and methods:** We examined samples from 94 patients (54 men and 40 women; median age, 70 years) at diagnosis who were prospectively enrolled between 2002 and 2008. All patients treated with R-CHOP. The pattern of FOXP3 protein expression was evaluated using immunohistochemistry in paraformaldehyde-fixed tissue samples. In addition, these samples were stained with antibodies for CD10, bcl-6 and MUM-1 via the tissue microarray to classify into subgroups.

**Results:** The median percentage of FOXP3+ cells was 91/mm² (range 4-2100/mm²). Patients with poor performance status (PS) and high serum lactate dehydrogenase (LDH) showed lower numbers of FOXP3+ cells (PS, \( P=0.014 \); LDH, \( P=0.0048 \)). Patients with high counts of FOXP3+ cells (>90/mm²) had better prognosis than those of low counts [5-year (5-y) overall survival (OS); 72.1% and 49.7% \( P=0.024 \), respectively]. Although no prognostic difference was observed between the GCB type and the non-GCB type (5-y OS: GCB 71.2%, non-GCB 53.1%, \( P=0.12 \)), low counts of the FOXP3+ cell and the non-GCB type patient were poorer prognosis than high counts and the non-GCB type (low 5-y OS, 31.2%; high 5-y OS, 69.8%; \( P=0.02 \)).

**Conclusion:** An increased count of the FOXP3+ tumor-infiltrating cell might predict better prognosis of DLBCL.

**P1 – 154** MAXIMUM STANDARD UPTAKE VALUE AT THE BIOPSY SITE DURING 18F-FUROUREDODEXYGLUCOSE POSITRON EMISSION TOMOGRAPHY DOES NOT PREDICT THE PROLIFERATION POTENTIAL OF TUMOR CELLS IN EXTRANODAL NATURAL KILLER/T-CELL LYMPHOMA, NASAL TYPE

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The proliferation potential of tumor cells is indicated by the proliferation of Ki-67, a nuclear antigen expressed by dividing cells. A high Ki-67 proliferation index (MIB-1-labeling index) is associated with poor prognosis in non-Hodgkin lymphoma, T-cell lymphoma, and localized extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKL). The maximum standardized uptake value (SUVmax) of the biopsy site during 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) reflects tumor aggressiveness in non-Hodgkin lymphoma cases. In ENKLs, a 100% positive rate of FDG-PET has been previously reported. Here, we evaluated the biopsy sites of patients with untreated ENKL to clarify the correlation between SUVmax at the biopsy site and the proliferation potential of tumor cells. Between 1998 and 2011, 22 patients were newly diagnosed with ENKL at Yokohama City University Hospital and Kanagawa Cancer Center. In 17 cases, the tumors were staged using PET or PET/computed tomography (CT), and biopsies were simultaneously conducted. Variations in SUVmax among institutions and the underestimations derived from small tumors, which are limitations of PET carried out in multicenter studies, were corrected by a phantom study using a NEMA IEC Body Phantom SetTM. The difference in the accuracy of SUVmax between the two institutions was less than 2%. We studied 15 extranodal biopsy specimens from 13 patients with untreated ENKL, for whom complete data were available. The biopsy specimens were reviewed by two hematopathologists (S.S. and K.T.), according to the World Health Organization (WHO) classification. The study comprised 10 men and 3 women, with a median age of 52 years (range: 18–82 years). We found that the SUVmax was not correlated with the MIB-1-labeling index (\( r = 0.33 \); \( P = 0.22 \)). In conclusion, this study indicates that the SUVmax during FDG-PET does not predict the proliferation potential of ENKLs.

**P1 – 155** EARLY RELAPSE IS ASSOCIATED WITH THE HIGH SERUM SOLUBLE INTERLEUKIN-2 RECEPTOR LEVEL AFTER THE SIXTH CYCLE OF R-CHOP CHEMOTHERAPY IN PATIENTS WITH ADVANCED diffuse LARGE B-CELL LYMPHOMA

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Diffuse large B-cell lymphoma (DLBCL) is the most common form of non-Hodgkin lymphoma. The present study assessed retrospectively the clinical significance of the serum soluble interleukin-2 receptor (sIL-2R) level in patients with advanced DLBCL. Twenty-one patients (age; range, 56–87, median, 73-year old, 14 males/7 females) were newly diagnosed as having advanced DLBCL (stages III and IV) based on pathological findings of the biopsy specimen and by using computed tomography and positron emission tomography between 2006 and 2009. All the patients received 6–8 cycles of the combination of CHOP (cytokinephamide, doxorubicin, vincristine and prednisolone) (R-CHOP) or THP-COP (pirarubicin, cyclophosphamide, vincristine and prednisolone) (R-THP-COP) and attained complete response at the end of the treatment. The follow-up period ranged between 12 and 73 months with the median of 37 months. The serum sIL-2R levels (normal range, 144–518 U/ml) were determined at least before and after the second and the sixth cycles of the chemotherapy were carried out. Although all the patients reached complete remission, six patients experienced the disease relapse within 1 year from the initiation of the treatment. sIL-2R levels before the chemotherapy ranged from 416 to 21300 U/ml (median 2609 U/ml). sIL-2R levels after the second cycle of the chemotherapy ranged from 276 to 1980 U/ml (median 675 U/ml). sIL-2R levels after the sixth cycle of the chemotherapy ranged from 364 to 822 U/ml (median 548 U/ml). The early relapse was significantly associated with the high sIL-2R levels at the sixth cycle of the treatment, whereas the sIL-2R levels were low in the patients with the durable remission. sIL-2R levels at the disease onset or after the second cycle of the treatment were not correlated to the duration of the remission. Thus, the present study suggested that the sIL-2R levels after the sixth cycle of the chemotherapy might predict the early relapse in patients with advanced DLBCL.
Poster Session 23: Palliative and supportive care clinical analyze 1

P1 – 108 PNEUMOCYSTIS JIROVECII PNEUMONIA (PJP) IN NON-HIV INFECTED PATIENTS WITH SOLID TUMOR

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Background: There is a growing number of Pneumocystis jirovecii pneumonia (PJP) in non-HIV-infected population. Although it is a treatable infection, it can be fatal in severe cases. The purpose of this study was to describe the clinical characteristics and mortality of PJP in solid tumor patients.

Methods: The medical records of all patients with solid tumor in Department of Medical Oncology at Kameda Medical Center between 2008 and 2011 were retrospectively reviewed. The clinical and laboratory findings of the patients with a first proven episode of PJP were extracted. The diagnosis was made by microscopy with Diff-Quik staining and/or polymerase chain reaction of induced sputum or bronchoalveolar lavage fluid.

Result: Among the 1481 patients, there were five documented cases of PJP. The median age was 70 years (range 49–80). The underlying malignancies were lung cancer (two), gastric cancer (one), rectal cancer (one) and thymic carcinoma (one). Four patients had dyspnea, and one had fever. The median duration from the diagnosis of malignancy and the diagnosis of PJP was 10 months (range 3–32). The patients’ performance statuses (number) were 1 (3), 3 (1) and 4 (1), respectively. The median lymphocyte count was 1155/mm³, β₂-g-glucan levels were elevated in four patients (median level: 26 pg/ml). Within 30 days before the diagnosis of PJP, four of five patients were receiving corticosteroids (dexamethasone) at median cumulative 30-day dose of 36 mg. No patient was on PJP prophylaxis. One patient died of PJP and others recovered. The radiographic findings of all patients were diffuse bilateral interstitial infiltrates.

Conclusion: The incidence of PJP in solid tumor patients is higher than expected. Although the number of cases was small, the mortality rate was 20% among the documented cases. This study suggests the importance of PJP prophylaxis in patients with solid tumor who are receiving corticosteroid and of prompt diagnosis of PJP in such patients with diffuse pulmonary infiltrates.

P1 – 160 THE ESTIMATION OF LIFE-TIME FOR THE PATIENTS WHO ACQUIRED RESISTANCE TO STANDARD CHEMOTHERAPIES

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Background: Prognostication is important for the advanced cancer patients to make the most for the rest of their life. We examined the accuracy of oncologist clinical predictions of survival (CPS) and the factors that oncologists referred to in cancer patients who acquired resistance to the standard chemotherapies. We also examined how oncologists share the information about the survival with patients and their family.

Methods: Fourteen oncologists treating major adult solid malignancies (breast, lung, gastrointestinal, pancreatic, gynecologic cancer and sarcoma) participated in this observational prospective cohort study between October 2010 and October 2011. The oncologists were asked to fill in the questionnaire about CPS when patients acquired resistance to the standard chemotherapies.

Result: The data of 52 patients were available for analysis. The median CPS was 92 days (interquartile range (IQR), 61–168 days), and the median actual survival (AS) was 80 days (IQR, 35–148 days). The median difference between CPS and AS (CPS – AS) was 21 days (IQR, –26 to 50 days). The Spearman correlation between CPS and AS was 0.66 (P < 0.001) and they were highly significantly associated. The proportion of patients with [CPS – AS] > 7, 14 and 28 days were 6, 14 and 42%, respectively. Although age, oral intake, the number of chemotherapy regimens and the prognostic factors that oncologists referred to were not related to [CPS – AS], Eighteen patients (35%) were informed about the prognosis and 37 patients (71%) were provided with information about the palliative care unit. Thirty-three patients (64%) received best supportive care alone and 18 patients (35%) received further chemotherapies.

Conclusions: Oncologists’ predictions generally correlated with AS. As long as the prediction of survival is based on the prognostic factors that oncologists referred to, CPS can be correct to within as least 4 weeks.

Poster Session 24: Palliative and supportive care clinical analyze 2

P1 – 161 PALLIATIVE CARE FOR BONE AND SOFT TISSUE SARCOMA PATIENTS

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Background: There have been few studies on palliative care for patients with bone and soft tissue sarcoma due to its low prevalence. We report 19 cases of patients with bone and soft tissue sarcoma who were consulted to the palliative care team.

Method: We retrospectively reviewed all medical records of patients with bone and soft tissue sarcoma who were consulted to the palliative care team.

Result: Nineteen patients (6 males and 13 females) were reviewed in this study. The median age was 50 years (23–80). The underlying malignancies were lung cancer (6), gastrointestinal stromal tumor (2), and bowel perforation (n = 6), followed by bleeding of the tumor (n = 7), intractable pain (n = 1). The sites of metastases were lung (n = 11), pelvic viscera (n = 8), liver (n = 7), and bone (n = 7). The median number of chemotherapy regimens was 2 (0–5). The most common life-threatening complication was respiratory failure (n = 6), followed by bleeding of the tumor (n = 3), pulmonary embolism (n = 2), and bowel perforation (n = 1). Reasons of consultation were psychological support (n = 7), intractable pain (n = 6), and lymphedema (n = 6). Fifteen patients (79%) used opioids, including fentanyl patch 33%, fentanyl continuous infusion 20%, oral oxycodone 20%, oral morphine 13%, and morphine continuous infusion 13%. One patient used an antidepressant drug.

Conclusions: The patients with bone and soft tissue sarcoma tended to be highly distressed by the absence of enough information about their disease and standard chemotherapy in the early stage of therapy, therefore they needed psychological support. In the middle and the late stage of disease, they tended to have life-threatening complications that worsen the prognosis.

P1 – 169 THE EVALUATION OF RENAL FUNCTION IN PATIENTS TREATED WITH REDUCED-DOSE DOCETAXEL, CISPLATIN AND 5-FLUOROURACIL

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Purpose: To evaluate renal function in patients treated with reduced-dose DCF (DTX 60 mg/m² on day 1, CDDP 60 mg/m² on day 1 and 5FU 500 mg/m² on days 1–4).

Patients and methods: Ten patients with unresectable esophageal cancer and two patients with unresectable gastric cancer were planned to administer four courses of reduced-dose DCF every 3 weeks. In baseline, the glomerular filtration rate (GFR) was estimated with creatinin clearance using a 24-h urine collection (CrCl) and the Cockcroft–Gault (C-G) method. We used innovator cisplatin formulation (Randa: Nichon Kayaku). We prepare a solution consisting of 1000 ml of isotonic saline plus 20 ml of potassium chloride. We administer intravenously 1000 ml of this solution over 2 h before and following the cisplatin administration. We used magnesium sulfate and mannitol for renal protection and 2000 ml of hydration from days 2 to 4. Serum creatinine and GFR with the C-G method were measured until 1 month after the completion of reduced-dose DCF.

Result: Ten patients completed four courses of reduced-dose DCF and two patients discontinued after two courses because of disease progression. In baseline, the median CrCl was 98.8 ml/min (58.7–150.6) and the median GFR with the C-G method was 77.6 ml/min (46.2–121.6) and the correlation coefficient of both was 0.7253. Grade 1 and 2 creatinine elevation was observed in 8%, respectively. The median creatinine increased was 0.11 mg/dl (0.00–0.38) and the median GFR decreased with the C-G method was –1.33 ml/min (–10.60 to 23.91).
Background: Even after prophylactic cranial irradiation (PCI), many small-cell lung cancer (SCLC) patients succumb to brain metastasis. Brain metastasis after PCI is an unsolved issue in SCLC in terms of its dismal prognosis and the limitation of further treatment options. Regarding the treatment option, it is not determined whether re-whole brain radiotherapy (re-WBRT) is safe or gamma-knife surgery (GKS) has its role in SCLC. We investigated which treatment option could be recommended as the up-front therapy to improve survival for SCLC patients with brain metastasis who were previously treated with PCI.

Methods: The medical records were reviewed for SCLC patients who experienced brain metastases after receiving PCI from 2000 to 2010. We compared overall survival according to the modality of up-front therapy. Overall survival was determined as time from brain metastasis to death due to any cause.

Results: In total, 245 patients had received PCI in a state of limited disease (n = 204) or extensive disease status (n = 41). Among them, 47 (19.2%) experienced brain metastases: 16.7% (34/204) in LD and 31.7% (13/41) in ED. At the time when brain metastasis developed, extracranial disease was also on progressing stage in 19 patients (40.4%). The modality of up-front therapy for brain metastasis was as follows: 17 (36.1%) got GKS, 14 (29.8%) re-WBRT, 7 (14.9%) up-front chemotherapy without local therapy, and 9 (19.1%) did not receive any further treatment. The median overall survival after brain metastasis was 4.9 months. Among 31 patients who received GKS or re-WBRT, 10 patients received at least one subsequent chemotherapy in their lifetime after GKS (6/17, 35.3%) or re-WBRT (4/14, 28.6%). The median survival of GKS, re-WBRT and chemotherapy was 14.3, 3.9 and 6.0 months (P = 0.24), which showed the tendency favoring for up-front GKS. Although it failed to meet statistical significance.

Conclusions: The up-front GKS showed longer survival in patients who experienced brain metastasis after PCI for SCLC, compared with re-WBRT or chemotherapy. However, the number of participants was too small to get confirmatory results requiring a prospective therapy to demonstrate the role of GKS in this setting.

Poster Session 26: Lung cancer SCLC

P2-001

THE TREATMENT OPTIONS OF RECURRENT BRAIN METASTASIS AFTER PROPHYLACTIC CRANIAL IRRADIATION IN PATIENTS WITH SMALL-CELL LUNG CANCER

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Conclusion: Although CrCl tended to overestimate GFR than the C-G formula, the minimum maybe, because we used innovator cisplatin formulation and we managed with the optimal hydration method for renal protection.

Poster Session 25: Bone and soft tissue tumor

P1-172

MESENCHY MAL STEM CELLS AFFECT THE RESPONSE OF OSTEOSARCOMA CELLS TO STRESS-RELATED NEUROTRANSMITTEDS UNDER HYPOXIA

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Conclusion: Although CrCl tended to overestimate GFR than the C-G formula, the minimum maybe, because we used innovator cisplatin formulation and we managed with the optimal hydration method for renal protection.
effective for LCNEC, the standard chemotherapy has not been established for LCNEC. Accordingly, patients with LCNEC have been administered chemotherapy which was the standard therapy for small-cell lung cancer (SCLC). To evaluate the efficacy of chemotherapy for the LCNEC, we assessed tumor response to chemotherapy and survival in patients with LCNEC and SCLC.

**Patients and methods:** Patients with histologically or cytologically confirmed metastatic or recurrent LCNEC or ED-SCLC who received chemotherapy in our institution were eligible. The efficacy of chemotherapy was retrospectively evaluated on the basis of the overall response rate (ORR) and the overall survival.

**Results:** From January 1999 to August 2011, 14 patients with metastatic or recurrent LCNEC received chemotherapy in our institution. On the other hand, 122 patients with ED-SCLC were administered chemotherapy in the same period. Gender, age, and performance status were similar in the LCNEC and ED-SCLC groups. There were more never smokers in the LCNEC group than the ED-SCLC group. Patients with the ED-SCLC group had more metastatic sites than patients with the LCNEC group. In the first-line chemotherapy, 79% of patients with LCNEC and 92% with ED-SCLC received platinum-containing chemotherapy. The ORR of first-line chemotherapy was 57% and 58% for the LCNEC and ED-SCLC groups, respectively (P = 1.00). The median survival time was 11.8 months (95% CI: 4.0–14.5) in the LCNEC group and 11.8 months (95% CI: 10.5–14.1) in the ED-SCLC group, respectively. There was no statistical significance between both groups.

**Conclusion:** The efficacy of chemotherapy for LCNEC was similar to that for ED-SCLC in terms of tumor response and survival.

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A 77-year-old male with a history of smoking (B.I. 800) was diagnosed with lung adenocarcinoma. DNA analysis revealed a mutation of the epidermal growth factor receptor (EGFR) gene in exon 19 deletion in his bronchoscopic transbronchial biopsy specimens by the Cycleave method. During observation only, as wished by the patient, the tumor grew gradually and pleural effusion occurred. He was diagnosed with malignant pleural effusion, but EGFR gene mutation was not observed in that specimens by the PNA-LNA PCR clamp method. Treatment with gefitinib was started and the tumor size and pleural effusion remarkably decreased. After 4 weeks of treatment with gefitinib, a re-biopsy was done. We could find adenocarcinoma by bronchoscopy, but cancer cells were not observed in pleural effusion. When analysis of the EGFR gene was conducted, mutation was not observed in the pulmonary tissue by the RT-PCR method. Nowadays, we can use several EGFR gene mutation detection methods using the PCR technique, and each is almost equal in quality. But some reports showed that different results were received from different methods. We probably thought the result of pretreatment specimen from pleural effusion was false negative. The EGFR tyrosine kinase inhibitor (EGFR-TKI) such as gefitinib is a key drug for mutated-EGFR non-small-cell lung cancer. Therefore, we should avoid the loss of treatment opportunity with EGFR-TKI because of false-negative results.

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**Poster Session 28: Lung cancer case 2**

**GROWING TERATOMA SYNDROME OF THE LUNG SECONDARY TO NON-SEMINOMATOUS GERM CELL TUMOR OF THE TESTIS: A CASE REPORT**

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We report a rare case of the growing teratoma syndrome (GTS). The patient was a 37-year-old man diagnosed as having a mixed germ cell tumor of the right testis. After resection of the right testis, the patient developed multiple lung metastases and chemotherapy was administered. However, in spite of the normalization of the serum AFP level, the lung metastases continued to increase in size. The lung metastases were successfully resected and pathological examination revealed the diagnosis of a mature teratoma. GTS defined as an enlarging tumor mass during or after chemotherapy in the case of germ cell tumor, with the normalization of the serum AFP. The total surgical resection of the mass yielded good result, and the recognition of this syndrome is important for successful treatment.

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**Poster Session 27: Lung cancer case 1**

**CBDDA + Pemetrexed + Bevacizumab and Its Maintenance Chemotherapy as a Second Line in a Case of Sole Breast Metastasis from Lung Adenocarcinoma After Complete Response by Gefitinib as a First-Line Chemotherapy**

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A 58-year-old female was admitted for examination of pleural effusion and cardiac tamponade which was caused by lung adenocarcinoma possessing a mutation of the EGFR gene (deletion of exon 19). She was treated by gefitinib (250 mg/body/day) as a first-line chemotherapy, and its effect was determined CR. After 12 months, CEA was gradually increasing and she complained of right breast mass. With core-noodle biopsy, the breast tumor was pathologically diagnosed as recurrence and sole metastasis from lung adenocarcinoma, which was treated by CBDDA + pemetrexed + bevacizumab (AUC6 + 500 mg/m2 + 15 mg/kg) as a second-line chemotherapy and its maintenance chemotherapy (pemetrexed + bevacizumab) is still being undergone. The case of a pt with a breast metastasis from lung adenocarcinoma is very rare. Further, immunohistochemical study is very useful to diagnose. Taken together, in the case of a patient with breast tumor with present or previous malignancy, the metastatic breast tumor should be considered in differential diagnosis.
contribute to a long-term survival in some patients of thymic carcinoma. It suggests that the combination of surgery, irradiation and/or chemotherapy could be effective in thymic carcinomas and experienced three long-term survivors in thymic carcinoma. We conducted a retrospective review of 11 cases of thymoma and thymic carcinoma were 533 days (range 219–2302), and three patients survived over 3 years.

Conclusion: The addition of bevacizumab to chemotherapy showed significant benefits in progression-free survival and overall survival in patients with advanced NSCLC.

Poster Session 29: Lung cancer/mediastinal tumor/Mesothelioma

P2 – 020

CLINICAL SIGNIFICANCE OF PLEURAL EFFUSION MESOTHELIN IN MALIGNANT PLEURAL MESOTHELIOMA

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Background: Malignant pleural mesothelioma (MPM) is an aggressive malignant tumor of mesothelial origin associated with asbestos exposure. MPM has a limited response to conventional chemotherapy and radiotherapy, so the early diagnosis of MPM is very important. This study investigated the pleural effusion mesothelin levels in patients with MPM and compared them with those of a population with a non-malignant pleuritis or lung cancer involving malignant pleural effusion.

Methods: The pleural effusion mesothelin concentrations were measured in 45 MPM patients and 53 non-MPM individuals (24 individuals with non-malignant pleural effusions and 29 individuals with lung cancer involving malignant pleural effusion).

Results: This study demonstrated that patients with MPM had significantly higher pleural effusion mesothelin levels than a population with non-malignant pleuritis or lung cancer involving malignant pleural effusion. The difference in overall survival between the groups with pleural effusion mesothelin levels lower and higher than the assumed cutoff of 10 nM was significant.

Conclusions: The data suggest that the pleural effusion mesothelin concentration could be useful as an aid for the diagnosis of MPM.

P2 – 021

ELEVEN THYMIC EPITHELIAL TUMORS: OUR INSTITUTION EXPERIENCE

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Background: Thymoma and thymic carcinoma are rare tumors. Due to their rarity, no optimal treatment has been determined. We report here on 11 such patients about their background characteristics, treatment strategy and its outcome.

Methods: We retrospectively reviewed the medical records of patients with thymoma and thymic carcinoma treated at our institution, between 1998 and 2011.

Result: There were seven men and four women, with the median age of 56 years (range, 32–72). All thymic epithelial tumors arose in anterior mediastinum, and the median tumor size was 7 cm (range, 3–10). Two patients showed myasthenia gravis. Clinical symptoms included neck or shoulder pain in three patients, dyspnea in three patients and blepharoptosis in two patients. Histologically, four patients had thymomas, whereas seven had thymic carcinomas, and according to the WHO histological classification of their lesion, i.e. low-risk tumours (types A, AB and 0), and the high-risk group comprised 13 cases (type B2; 7; type B3, 3; thymic carcinoma, 3). The SUV-max values of the low- and high-risk tumours were 3.69 ± 0.51 and 6.19 ± 3.13, respectively, and this was a significant difference. For the differential diagnosis of low- and high-risk tumours, sensitivity and specificity were 92.3 and 83.3%, respectively, when an SUV-max of 3.5 was used as a cutoff.

Conclusions: FDG-PET is a useful method for distinguishing histological types of early-stage thymic epithelial tumours.

Poster Session 30: Lung cancer NSCLC

P2 – 026

THE COMBINATION CHEMOTHERAPY OF GEMCITABINE AND CARBOPlatin-BEvacizumAB IN PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG Cancer

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Background: The addition of bevacizumab–pactaxted and carboplatin showed significant benefits in progression-free survival and overall survival in patients with advanced non-small-cell lung cancer. We are conducting a prospective study about safety and efficacy of combination chemotherapy with gemcitabine and carboplatin–bevacizumab (GC + BV) in previously untreated patients with advanced metastatic NSCLC.

Methods: Between April 2010 and January 2012, a total of 35 patients with recurrent or advanced NSCLC (stage IIIB or IV) were treated with the GC + BV regimen. The regimen consists of gemcitabine of 1000 mg/m2 on days 1 and 8, carboplatin of AUC 5 and bevacizumab of 15 mg/kg on day 1. Treatment repeats every 3 weeks up to six cycles, followed by bevacizumab until disease progression or intolerable toxicity.

Results: Thirty-four patients were male. The median age of patients was 68 (55–79) years. Twenty-six patients were stage IV or recurrent disease and 9 were IIIB. Fifteen (60%) patients were adenocarcinoma (12, squamous cell carcinoma; 8, others). Twenty-four (68%) patients had ECOG PS of 0–1. The overall response rate was 46% with no complete response and 16 partial responses. Grade 3 and 4 neutropenia were 16 and 1%, respectively. Clinically significant hemorrhagic events were not identified till now. There was one treatment-related death (septic shock with neutropenia during the first cycle). Non-hematologic toxicities were mild and manageable, but two patients complained grade 3 general weakness and one patient experienced grade 4 pneumonia. The median PFS was 5.7 months (95% CI, 3.69–6.43 months).

Conclusions: The addition of bevacizumab–gemcitabine and carboplatin in the treatment of selected patients is effective and tolerable in NSCLC including squamous cell carcinoma. This is ongoing study and we present preliminary results.
AN INVESTIGATION INTO P/B-MAINTENANCE THERAPY FOLLOWING COMBINED THERAPY WITH CARBOPLATIN (C) + PEMETREXED (P) + BEVACIZUMAB (B) AS PRIMARY TREATMENT AGAINST NON-SQ NSCLC

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Background: After performing the PARAMOUNT study, the significant prolongation of PFS was observed when conducting maintenance therapy with the single agent of P alone following cisplatin (CDDP) + P therapy. Upon an AVAPERI study, P/B-maintenance therapy exhibited a better PFS than the single agent of B alone following CDDP/P/B.

Purpose: The safety and efficacy was investigated regarding conducting P/B-maintenance therapy following primary treatment with C/P/B.

Methods: C AUC 5 + P 500 mg/m² + B 15 mg/kg were administered in 3-week intervals at a maximum of six courses to PS 0–3, stage IV, non-Sq NSCLC patients of ≥20 with no history of prior treatment who maintained adequate organ function. Maintenance therapy with P/B was conducted in non-PD cases at 3-week intervals until they became PD.

Outcome: There were seven cases (December 2009 to November 2010) of men/ women: 5/2, with a median age of 64 years old (74–76), PS 0/1/3: 2/3/2 and adenocarcinoma/large cell carcinoma: 6/1. The antitumor effect was: CR/PR/SD/PD: 0/5/1/1, RR = 71%, median PFS = 8.9 months and OS = 15 months, which was slightly better compared with the RR = 66%, PFS = 8.4 months of 17 cases that simultaneously underwent P following C/P/B in our institute. Regarding toxicity, neutropenia with G2 or more tended to be common compared with the C/P group, but other hematotoxicities were to the same extent. Two cases of G2 hypertension and one case of G2 ILD were observed with non-hematological toxicity, but it was rapidly improved by steroids. Among the seven cases, six cases completed the six courses of C/P/B, then switched over to P/B-maintenance therapy.

Conclusion: C/P/B therapy exhibited high efficacy and safety, thus suggesting that it may become one regimen for the primary treatment of non-Sq NSCLC.

Poster Session 31: Lung cancer NSCLC 4

DOXETAXEL MONOTHERAPY COMPARED WITH CARBOPLATIN AND PACLITAXEL DOUBLET CHEMOTHERAPY IN ELDERLY PATIENTS WITH NON-SMALL-CELL LUNG CANCER

Department of Respiratory Medicine

Background: Docetaxel monotherapy (D) is recommended to treat advanced non-small-cell lung cancer (NSCLC) in fit elderly patients in Japan; however, carboplatin and paclitaxel doublet chemotherapy (CP) was also reported to be associated with survival benefits compared with monotherapy. We compared a docetaxel monotherapy regimen with carboplatin and paclitaxel doublet chemotherapy in elderly patients with NSCLC.

Methods: We retrospectively examined overall survival (OS), progression-free survival (PFS) and response rate (RR) in advanced NSCLC patients aged 70 or over who received D alone or CP as a first-line therapy between April 2002 and December 2010 at our institution.

Results: Sixteen patients received D and 39 received CP. The characteristics of the each group were as follows: median age 75 (70–81) and 76.5 (70–84) years; male/ female 62/38 and 75/25%; adenocarcinoma/squamous cell carcinoma/undifferentiated carcinoma 54/44/2 and 63/37/0%; PS 0/1/2/3: 23/56/13/8 and 31/63/6/0%. The median number of treatment cycles was two in both groups. Antitumor effects were as follows: PR/SD/PD/NE 36/31/25/8 and 25/13/56/6% (P < 0.05); the median PFS 643 (71–84) and 585 (48–1122) days. One treatment-related death was observed in the CP group.

Conclusion: Although the RR was higher in the CP group, there were not any differences in PFS and OS between D and CP groups. Both D and CP could be used as a treatment in elderly patients with NSCLC.

EFFICACY AND SAFETY OF FIRST-LINE PLATINUM-BASED ADJUVANT CHEMOTHERAPY IN PATIENTS WITH POST-OPERATIVE RECURRENCE AFTER PLATINUM-BASED ADJUVANT CHEMOTHERAPY

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Background and aim: Several studies suggest that cisplatin-based adjuvant chemotherapy improves survival in patients with completely resected non-small-cell lung cancer in stage II and III; thus, this chemotherapy is recognized as a global standard regimen. However, the efficacy and safety of first-line platinum-based chemotherapy in patients with post-operative recurrence after platinum-based adjuvant chemotherapy has not been fully assessed. The aim of this study is to assess these clinical outcomes of platinum-based chemotherapy in patients with post-operative recurrence.

Subjects and methods: Clinical records of patients with post-operative recurrence who received platinum-based chemotherapy as first line after platinum-based adjuvant chemotherapy at Juntendo University Hospital and Shizuoka Cancer Center between April 2008 and December 2011 were reviewed, and the clinical efficacy and toxicity were retrospectively evaluated.

Result: A total of 11 patients were included in this study. The median age was 61 years (range, 36–71 years). Five patients were female. Eight patients were PS 0, the others were PS 1. Adjuvant chemotherapy regimens were CDDP + VNR in five patients, CBDCA + GEM in four patients, CBDCA + PTX in one patient and CBDP + Ts-1 in one patient. 72.7% of patients received at least three cycles of adjuvant chemotherapy. The median recurrence-free survival was 495 days (range, 98–1358 days). First-line chemotherapy regimens were CDDP + PEM in six patients (including one patient with a combination of VEGF-TKI), CBDCA + PTX + Bev in three patients, CBDP + VNR in one patient and CBDP + DTX in one patient. 63.6% patients received at least three cycles of first-line chemotherapy. The overall response rates and the disease control rates were 27.3 and 72.7% (CR/PR/SD/PD:NE 0/3/5/0), respectively. The median overall survival was 841 days (range, 210–1918). Two patients (16.7%) were dropped out. The receiving dose was ruled because of toxicity in four patients (36.4%).

Conclusion: The first-line platinum-based chemotherapy was effective, but highly toxic in patients with post-operative recurrence after platinum-based adjuvant chemotherapy.

BEVACIZUMAB-ASSOCIATED HEMOPTYSIS IN CARCINOID TUMOR METASTASES: A CASE REPORT

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A man in his 70s suffering from recurrent sigmoid colon cancer with multiple metastases was treated using tegafur/gimeracil/oteracil potassium/irinotecan (CPT-11) (16 cycles) as a first-line therapy, modified 5-FU/leucovorin/oxaliplatin as a second-line therapy and 5-FU/leucovorin/oxaliplatin (FOLFIRI)/bevacizumab as a third-line therapy. FOLFIRI and bevacizumab had to be discontinued after 47 cycles because of atypical pneumonia. Cetuximab/CPT-11 was used as a fourth-line regimen, but metastasis continued after two cycles. We used FOLFIRI-bevacizumab as a fifth-line therapy because a computed tomography (CT) scan did not show pneumonia, and his metastasis had been well controlled previously with this regimen. After 58 courses, CT scan showed no pneumonia, and there was no increase in lung metastases. On day 18 of 59 courses, he developed hemoptysis unexpectedly at his home, and he was brought to our hospital. On emergency CT scan, a cavity in the lung field was detected in the lung field where lung metastasis had occurred, and Staphylococcus aureus was found in the patient’s sputum. Intensive antibiotic therapy was initiated; however, the patient died three days later because of severe hemoptysis. Bevacizumab, a monoclonal antibody against a vascular endothelial growth factor, is used in several types of carcinoma, namely the lung, breast and colorectal cancers. In the phase trials of lung cancer, there were several reports of hemoptysis associated with bevacizumab, but there have been few reports on colorectal cancer. We reported a case of bevacizumab-associated hemoptysis in colorectal carcinoma with lung metastasis and reviewed the associated literature.
of adding on Beva in November, and Beva + m-FOLOFOX6 was carried out. Complications of hypertension were seen on day 4, and headache, convulsions and disturbance of consciousness on day 5 after chemotherapy. MRI of the brain revealed bilateral high signal intensities of posterior lobes on T2 weighted and FLAIR images without enhancement. She was diagnosed as RPLS and referred to our department. She was treated with antihypertensive and anticonvulsive therapy. Her symptoms entirely disappeared after 12 days. The causing agent of RPLS was not clear, but we administered a single agent, CPT-11 which is one of the key drugs for colorectal cancer and then possible to treat with FOLFIRI safely. Medical oncologists should be aware that multidrug chemotherapies may increase the risk of fatal neurological complications like RPLS.

Poster Session 33: Gastrointestinal cancer case 4

P2 – 051 IMPRESSIVE CASES OF ADVANCED GASTRIC CANCER SUCCESSFULLY MANAGED WITH TRASTUZUMAB CONTAINING CHEMOTHERAPY

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As a result of the TeGA trial, trastuzumab in combination with capcitabine-cisplatin (XP) chemotherapy is now considered a new standard option for patients with HER2-positive advanced gastric cancer. We report three cases that showed marked tumor shrinkage with the induction of XP-trastuzumab chemotherapy in a practical setting. Case 1: A 68-year-old man with gastric papillary adenocarcinoma (HER2 status IHC 3+, FISH positive) and huge liver metastases produced α-fetoprotein, received four cycles of XP-trastuzumab chemotherapy. Although CT scan revealed shrinkage of the metastatic lesions after one course of the treatment, the lesions progressed after four courses. She underwent treatment with doxorubicin-ifosfamide as second-line chemotherapy and doxorubicin-cisplatin as third-line chemotherapy. The metastatic lesions progressed rapidly and she died 9 months after diagnosis.

P2 – 052 A CASE REPORT OF ADVANCED PANCREATIC NEUROENDOCRINE TUMOR TREATED WITH CHEMOTHERAPY FOR CISPLATIN CONTAINING RESIEMEN FOLLOWED BY EVEROLIMUS IN COMBINATION WITH OCTREOTIDE LAR

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Pancreatic neuroendocrine tumor (P-NET) accounts for less than 5% of all pancreatic tumors. Treatment options for advanced P-NET are somewhat limited. At this time, the standard therapy for advanced P-NET is not exist. Everolimus, which targets the mammalian target of rapamycin (mTOR), has recently been approved for patients with advanced P-NETs. We herein present a case of P-NET treated with chemotherapy for the cisplatin–etoposide regimen followed by everolimus in combination with octreotide LAR. A 71-year-old female was referred to our hospital with tumor in the tail of the pancreas with the multiple liver metastasis. The dynamic study of computed tomography (CT) scan showed hypervascular tumors on the early phase in the pancreatic tail and liver, both of which were the same enhanced pattern. No hormonal abnormalities demonstrated. Endosonography-guided fine needle aspiration (EUS-FNA) was undertaken to the pancreatic lesion. The cytology and immunological examination suggested both synaptophysin and chromogranin A positive, which led to the diagnosis with class III neuroendocrine tumor. Even histological examination was not carried out, she was diagnosed with stageIV P-NET because imaging studies had already revealed liver metastasis. She began to be treated with systemic therapy of cisplatin–etoposide resin similar to that used for small-cell lung cancer and octreotide LAR 30 mg, a long acting somatostatin analog, was given as a intramuscular (IM) injection every 28 days. After receiving two courses cisplatin–etoposide resin, the CT scan showed a marked increase in the tumor size in the liver and found to be progressive disease. Cisplatin–etoposide resin were switched to everolimus 10 mg PO daily with octreotide LAR 30 mg IM every 28 days continued. At the time of submission of this abstract, she has been still treated with everolimus–octreotide LAR.

Poster Session 34: Gastrointestinal cancer gastric cancer 1

P2 – 057 REG I: IS A BIOMARKER TO PREDICT POOR RESPONSE TO CHEMOTHERAPY WITH S-1+CISPLATIN IN PATIENTS WITH METASTATIC GASTRIC CANCER

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Background: Treatment with S-1-cisplatin is established as a standard first-line treatment of patients with unresectable metastatic gastric cancer in Japan. However, the useful biomarker to predict patients’ response to this treatment remains unclear. We investigated the clinicopathological factors related to the response to S-1-cisplatin treatment in patients with unresectable metastatic gastric cancer. Moreover, we examined whether REG I, an antiapoptotic factor, could be a useful biomarker to predict the response to chemotherapy in these patients.

Patients and methods: Seventy patients with stage IV gastric cancer received first-line chemotherapy with S-1-cisplatin. We investigated the relationship between clinicopathological factors and duration of progression-free survival. REG I expression was evaluated using reverse transcriptase-polymerase chain reaction before chemotherapy, and its relationship to clinicopathological factors was also investigated.

Results: The median progression-free survival (PFS) of all patients was 5.4 months. In patients with squarible type of gastric cancer, REG I tended to be shorter than that...
in patients with non-squamous type of gastric cancer (P = 0.058). Of the 70 gastric cancer tissues, 19 (27%) were positive for REG Ig protein. Univariate and multivariate analyses revealed that REG Ig expression was independently predictive of worse progression-free survival [hazard ratio (HR) 4.00, P = 0.008]. None of patients with REG Ig-positve gastric cancer responded to chemotherapy.

**Conclusion:** REG Ig may be a reliable biomarker to predict the poor response to chemotherapy with 5-1-cisplatin in patients with metastatic gastric cancer.

**Results:** Although there were no significant difference between age, PS, histology and prior chemotherapy, male patients and number of metastatic organs were more in arm CM. The overall response rate in arm CM was 19%, and in arm C was 10.5%. The median progression-free survival was 3.8 months in arm CM versus 3.8 months in arm C. The median overall survival of arm CM versus arm C was 9.6 versus 11 months. Major grade 3/4 adverse events in arm CM versus arm C were as follows: neutropenia (45 versus 22%), anemia (36 versus 43%), lefibre neutropenia (13 versus 12%), anorexia (14 versus 8.7%).

**Conclusions:** The treatment effect of CPT-11–MMC was equivalent to CPT-11 alone in patients with AGC refractory to fluoropyrimidine and platinum. CPT-11–MMC was associated with a higher incidence of grade 3 or 4 adverse events than CPT-11 alone.

**Material and methods:** Between 2002 and 2011, we retrospectively reviewed the medical records of 138 patients with metastatic gastric cancer in our institute. We investigated incidence of skeletal metastases, percentage of patients who developed skeletal-related events (SREs) and differences in the therapeutic outcome between patients with and without skeletal metastases.

**Results:** 23 patients (median age: 59.5 years; range from 29 to 76) were found to have skeletal metastases during their clinical course. Almost all patients have multiple sites of disease that appeared osteoblastic on radiography. Among them, only three (13%) patients experienced SREs (two had spinal cord compression and one had pathological fracture), because most of the patients died of systemic disease progression before the clinical development of SREs. Of the 23 patients, 18 patients (78.3%) had skeletal metastases at the time of initial diagnosis, and 5 patients (21.7%) developed skeletal metastases later in the course of their disease. For 18 patients who presented skeletal metastases at the diagnosis, the median survival time (MST) was 7.4 months, whereas it was 11 months for those without such metastases. Hematological complications, including microangiopathic hemolytic anemia (MAHA) and disseminated intravascular coagulation (DIC), occurred more often with skeletal metastases than with non-skeletal metastases (44 versus 0.9%, respectively), which may relate to the shorter survival of patients with skeletal metastases.

**Conclusions:** Our study suggests that the prognosis of gastric cancer with skeletal metastases is poor. Earlier identification and the novel treatment of skeletal metastases would be crucial for improving survival in this patient group.

**Poster Session 35: Gastrointestinal cancer gastric cancer 2**

**P2 – 069 SKELETAL COMPLICATIONS AND SURVIVAL IN GASTRIC CANCER PATIENTS WITH SKELETAL METASTASES**

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**Background:** The skeleton is one of the most frequent sites for metastases in patients with advanced cancer. Several guidelines have been proposed covering diagnosis and management of skeletal metastases in patients with breast and prostate cancer. As skeletal metastases in gastric cancer are less frequent events, there have been limited reports that evaluated the incidence, influence on survival of skeletal metastases and the role of bisphosphonate in the treatment of advanced gastric cancer.

**Material and methods:** Between 2002 and 2011, we retrospectively reviewed the medical records of 138 patients with metastatic gastric cancer in our institute. We investigated incidence of skeletal metastases, percentage of patients who developed skeletal-related events (SREs) and differences in the therapeutic outcome between patients with and without skeletal metastases.

**Results:** Of the 138 patients, 23 patients (median age: 59.5 years; range from 29 to 76) were found to have skeletal metastases during their clinical course. Almost all patients have multiple sites of disease that appeared osteoblastic on radiography. Among them, only three (13%) patients experienced SREs (two had spinal cord compression and one had pathological fracture), because most of the patients died of systemic disease progression before the clinical development of SREs. Of the 23 patients, 18 patients (78.3%) had skeletal metastases at the time of initial diagnosis, and 5 patients (21.7%) developed skeletal metastases later in the course of their disease. For 18 patients who presented skeletal metastases at the diagnosis, the median survival time (MST) was 7.4 months, whereas it was 11 months for those without such metastases. Hematological complications, including microangiopathic hemolytic anemia (MAHA) and disseminated intravascular coagulation (DIC), occurred more often with skeletal metastases than with non-skeletal metastases (44 versus 0.9%, respectively), which may relate to the shorter survival of patients with skeletal metastases.

**Conclusions:** Our study suggests that the prognosis of gastric cancer with skeletal metastases is poor. Earlier identification and the novel treatment of skeletal metastases would be crucial for improving survival in this patient group.
CURRENT SITUATION OF ADJUVANT CHEMOTHERAPY FOR STAGE II/III GASTRIC CANCER IN OUR HOSPITAL
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Background: We retrospectively analyzed the efficacy of adjuvant chemotherapy in patients with stage II/III gastric cancer. The standard of care for stage II/III gastric cancer in Japan is curative gastrectomy and adjuvant chemotherapy with S-1 for 1 year. We retrospectively analyzed the feasibility and the outcome of adjuvant chemotherapy in our hospital.

Method: We analyzed about the feasibility and outcome of adjuvant chemotherapy with stage II/III gastric cancer patients who had undergone curative gastrectomy in our hospital between 2007 and 2010.

Results: A total of 90 patients were evaluated. Patients' characteristics are shown each of the following: median age, 68 years (range: 43–82); sex (male/female), 61/29; stage (II/III), 60/30; pathology (differenitated/undifferenitated), 48/42. The completion rate with adjuvant chemotherapy was 67% (60/90). Thirty patients discontinued adjuvant chemotherapy due to toxicity (n = 11.37%), recurrence (n = 12.40%) and other reasons (n = 7.30%). Twenty-two patients experienced recurrence. Of the 22 patients, 16 patients experienced early recurrence (recurrence within 6 months after adjuvant treatment). The other six patients experienced non-early recurrence. The median period of observation from recurrence was 2.8 months (range: 0–22.5). The median survival time of early recurrence patients was 6.8 months (range: 0.4–10.0) and non-early recurrence was 3.3 months (range: 1.4–16.7; log-rank P = 0.9974).

Discussion: The completion rate with adjuvant chemotherapy with S-1 in our hospital is 67% that is equivalent to the report of ACTS-GC. It is unclear that the period of recurrence from last administration of S-1 makes effect to overall survival in this retrospective study.

Poster Session 37: Gastrointestinal cancer colorectal cancer 2

OXALIPLATIN-INDUCED HYPERSENSITIVITY REACTIONS IN PATIENTS WITH ADVANCED COLORECTAL CANCER IN A SINGLE HOSPITAL
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Oxaliplatin is a third-generation platinum agent indicated for the treatment of metastatic colorectal cancer. It is regarded as a high risk for the development of hypersensitivity reactions. Clinical data from 119 patients with colorectal cancer were analyzed, who were treated with oxaliplatin containing regimens (POLFOX4, mFOLFOX6, XeoloXELFOX) between April 2007 and January 2012. Eighty males and ninety females had hypersensitivity reactions. The 17 patients were 43–75 years (mean 65 years), total cycle number of therapy with oxaliplatin were 2–19 cycles (median 9 cycles). The severity of hypersensitivity reactions was assessed by using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Five cases had grade 1, 11 cases grade 2 and 1 case had grade 3 hypersensitivity reactions. An immediate hypersensitivity reaction showed itching, rash, stomachache, vomit and choking. Oxygen saturation was measured continuously. Hypoxemia was diagnosed for hypersensitivity reaction showed itching, rash, stomachache, vomit and choking.

Methods: Between January 2003 and December 2008, 860 patients with curatively resected stage II colon cancer were included. Deficient MMR (dMMR) was defined as tumors with MLH1 and/or MSH2 loss and others as proficient MMR (pMMR) by immunohistochemistry. Clinical risk (CR) factors were used for dividing patients into the high or the standard CR group.

Results: Of 860 patients, 14.7% showed dMMR, 42.4% had ≥1 CR factors, 85.8% received adjuvant chemotherapy. Age and gender were balanced with MMRS adjusted CR. There was no difference in terms of the recurrence rate (RR), relapse-free survival (RFS) or overall survival (OS) according to either MMR status or the CR group. Among CR factors, pT4 was the only prognostic factor associated with poor OS. Adjuvant chemotherapy was associated with lower RR, better RFS and OS. By multivariate analysis, neither MMR nor CR was related to RFS or OS, while adjuvant chemotherapy was associated with better OS. The estimated cumulative incidence of recurrence after adjusting competing risk was not affected by MMR, CR and adjuvant chemotherapy.

Conclusions: MMR status did not affect RFS and OS in patients with stage II colon cancer. Only pT4 among high CR factors did influence OS. Although adjuvant chemotherapy seemed to decrease RR and improve OS by conventional survival analysis, it was not associated with the cumulative incidence of recurrence after adjusting competing risk.

PREOPERATIVE CHEMORADIATION WITH S-1–OXALIPLATIN IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER: RESULTS OF A PHASE II STUDY AND THE ROLE OF DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING FOR PREDICTION OF PATHOLOGIC RESPONSES
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Background: We conducted a phase II study of preoperative chemoradiation (CRT) with S-1, a novel oral fluoropyrimidine, plus oxaliplatin in patients with locally advanced rectal cancer. The apprrent diffusion coefficient (ADC) of tumor was measured by diffusion-weighted magnetic resonance imaging (DW-MRI) and was evaluated as a predictive biomarker for pathologic responses.

Methods: The total radiotherapy dose was 50.4 Gy. Chemotherapy, as determined in our previous phase I study, consisted of oxaliplatin 50 mg/m² on days 1, 8, 22 and 5 and S-1 80 mg/m²/day on days 1–14 and 22–35. Total mesorectal excision was carried out within 6 ± 2 weeks. The primary end point was the pathologic complete response (pCR) rate. Tumor ADCs were measured by DW-MRI before and after CRT and were correlated with pathologic responses after surgery.

Results: A total of 38 patients was enrolled; 22 (57.9%) were men and the median age was 54 years (range: 28–76 years). Of the 35 patients who underwent curative surgery, 28 received sphincter-saving operations. No grade 4 toxicity was evident, and grade 3 toxicities included leukopenia (5.4%), diarrhea (5.4%), anorexia (2.7%) and nausea (2.7%). The pCR rate was 25.7% (8/33, 95% CI: 10.9–42.1), with additional 10 patients (28.6%) showing near total regressions of tumor. Tumor ADCs, as measured by DW-MRI, were calculated in 38 patients (including those who participated in the phase I study). The post-CRT ADC (1.52 ± 10−³ mm²/s ± 0.46) in the pCR group versus 1.07 ± 10−³ mm²/s ± 0.38 in the non-pCR group, P = 0.037 and the percentage change in ADC (44.5% in the pCR group versus −7.6% in the non-pCR group, P = 0.026) were significantly correlated with the pCR rate.

Conclusions: Preoperative CRT with S-1–oxaliplatin showed promising results in pathologic responses and favorable toxicity profiles. Tumor ADC, as measured by DW-MRI, seems to be useful in predicting responses.

A PHASE II TRIAL OF SALVAGE TREATMENT WITH GEMCITABINE AND S-1 COMBINATION IN HEAVILY PRETREATED PATIENTS WITH METASTATIC COLON CANCER
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Background: We conducted a phase II trial of gemcitabine with S-1 to evaluate the activity and toxicity of such a combination in heavily pretreated patients (pts) with metastatic colorectal cancer (mCRC) who have progressed after treatment with 5-fluorouracil, oxaliplatin and irinotecan.

Methods: Between December 2009 and November 2011, 23 pts (36 of planned) were enrolled, with the following characteristics: 12 males and 11 females, median age 57 years (28–72). S-1 was given orally (30 mg/m²) b.i.d. for 14 consecutive days and gemcitabine (1000 mg/m²) was given on days 8 and 15, every 21 days, until disease progression and for a maximum of nine cycles. The primary end point was the objective response rate (ORR).

Results: The median number of cycles was 4 (range 1–9). OR was 8.7% (95% CI: 0.0–20.2) and THE disease control rate was 56.5% (95% CI: 36.4–76.9) with two partial responses and eleven stable diseases. The median duration of disease control was 8.5 months.
Combination chemotherapy with gemcitabine and S-1 was well tolerated and efficacious for refractory mCRC pts. Toxicities included neutropenia (10.0%), anemia (3.3%), and diarrhea (6.7%). Peripheral neuropathy (limited to grade1/2) was observed in 43.3% of patients. There were no treatment-related deaths.

Conclusions: Combination chemotherapy with S-1 and Ox was moderately effective and well-tolerated in patients with refractory pancreatic cancer.

Background: Treatment with single-agent gemcitabine provides modest benefits in patients with metastatic pancreatic cancer. This study was carried out to determine the efficacy of gemcitabine in combination with oxaliplatin and capecitabine in patient with recurrent or metastatic pancreatic adenocarcinoma.

Methods: This was a prospective, single-arm, single-center study in patients with chemotherapy-naive metastatic or recurrent pancreatic adenocarcinoma. The primary end point was objective response. The study was designed as a Simons two-stage optimal design algorithm, divided into two stages. The first stage was to recruit up to 18 patients. If at least two objective responses were obtained, then a further 25 patients would be enrolled into the study. If no more than two responses were obtained among these 18 patients, the study would be halted. The study patients received gemcitabine 800 mg/m² on day 1, plus oxaliplatin 100 mg/m² on day 1 and capecitabine 800 mg/m²/day on days 1–7 every 14 days. Treatment was to be administered until disease progression or until withdrawal from the study due to unacceptable toxicity or other reasons.

Results: Eighteen patients were enrolled. The median age was 63 years (range, 39–73 years). Among these 18 patients, only one patient (5.5%) achieved an objective response. Therefore, the accrual terminated. The median time to disease progression was 2.1 months, and the median overall survival duration was 4.9 months. One-year overall survival rates were 35.3%. The most frequently reported grade 3 or 4 adverse events were asthenia (16.6%), and nausea (5.5%). There were no unexpected toxicities.

Conclusions: The addition of oxaliplatin and capecitabine to gemcitabine did not improve objective response in the first-line treatment of advanced pancreatic cancer patients.

The patients consisted of 22 men (73.3%) and 8 women with a median age of 64 years; 11 patients (36.7%) were in performance status (PS) of 0, 16 patients (53.3%) were in PS of 1, and 3 patients (10.0%) were in PS of 2. Seven patients (23.3%) had locally advanced disease, 19 patients (63.3%) had metastatic disease, and 4 patients (13.3%) had recurrent disease after surgical resection. A partial response was achieved in 3 (10.0%) and stable disease in 12 patients (40.0%)., giving a disease control rate of 50.0% with a median of two courses (range from 1 to 8). The median time to progression (TTP) and overall survival (OS) were 3.4 (95% CI: 1.3–5.3) months and 5.2 (95% CI, 2.4–6.8) months, respectively. Eleven patients (36.7%) were previously treated with gemcitabine monotherapy and received this combination chemotherapy as a second-line treatment. Nineteen patients (63.3%) had previously undergone monotherapy or combination chemotherapy containing gemcitabine, S-1, and/or irinotecan and received this combination chemotherapy as a third- or fourth-line treatment. TTP was significantly longer in patients without history of S-1 use (5.6 versus 2.8 months; P=0.005). The relative dose intensity of S-1 and Ox was 89.0 and 96.7% of the scheduled dose, respectively. Major grade 3/4 adverse events included neutropenia (10.0%), anemia (3.3%), and diarrhea (6.7%). Peripheral neuropathy (limited to grade1/2) was observed in 43.3% of patients. There were no treatment-related deaths.

Conclusions: Combination chemotherapy with S-1 and Ox was moderately effective and well-tolerated in patients with refractory pancreatic cancer.

Purpose: To evaluate the efficacy and safety of chemotherapy for unresectable stage IVb pancreatic cancer.

Patients and methods: We retrospectively reviewed 48 patients who received chemotherapy for unresectable stage IVb pancreatic cancer in our hospital from March 2005 to October 2011. The characteristics of the 48 cases were as follows: male, 25; female, 23; median age, 67 years; range, 44–83 years. ECOG performance status 0/1/2 = 6/40/2. Primary tumor arose in the head, body, tail and body to tail in 24, 13, 10 and 1, respectively. As a first-line chemotherapy, 36 patients were treated with gemcitabine (GEM) alone, 8 patients with S1 alone and 4 patients with both GEM and S1 (GEM/S1). In the GEM monotherapy, patients received GEM (1000 mg/m²) intravenously on days 1, 8 and 15, repeated every 28 days. In the S1 monotherapy, patients received S1 (80 mg/m²) orally from days 1 to 28, repeated every 42 days. In the GEM/S1 therapy, patients received GEM (1000 mg/m²) intravenously on days 1 and 8, and S1 (80 mg/m²) orally from days 1 to 14, repeated every 21 days. We evaluated the response rate, median survival time (MST) and adverse events. The Kaplan–Meier curves were used for statistical analysis.

Results: The response rate and disease control rate was 2.8 and 47.2% in GEM monotherapy, 12.5 and 50% in S1 monotherapy, and 50 and 50% in GEM/S1 therapy, respectively. MST was 8.4 months in GEM monotherapy, 7.8 months in S1 monotherapy, 4.0 months in GEM/S1 therapy, and there were no significant differences among these three therapies. Grade 3 toxicities were observed in GEM monotherapy (neuropathy, seven patients; neutropenia, five patients; thrombocytopenia, one patient) and in GEM/S1 therapy (neutropenia, one patient; appetite loss, one patient).

Conclusion: Although each regimen was safe and yielded the high disease control rate for stage IVb pancreatic cancer, further evaluation how to choose the regimen as a first-line therapy is needed.

Purpose: The aim of this study was to evaluate the efficacy and safety of S-1 and Oxaplatin (Ox) combination chemotherapy for patients with refractory pancreatic cancer.

Methods: Between March 2009 and October 2011, 30 patients with pancreatic cancer refractory to previous chemotherapy were included. S-1 was administered at 80 mg/m²/day for 14 consecutive days, followed by a 7-day rest, and Ox was administered at 100 mg/m² on day 1 every 3 weeks until disease progression or unacceptable toxicity was observed.

Results: The patients consisted of 22 men (73.3%) and 8 women with a median age of 64 years; 11 patients (36.7%) were in performance status (PS) of 0, 16 patients (53.3%) were in PS of 1, and 3 patients (10.0%) were in PS of 2. Seven patients (23.3%) had locally advanced disease, 19 patients (63.3%) had metastatic disease, and 4 patients (13.3%) had recurrent disease after surgical resection. A partial response was achieved in 3 (10.0%) and stable disease in 12 patients (40.0%), giving a disease control rate of 50.0% with a median of two courses (range from 1 to 8). The median time to progression (TTP) and overall survival (OS) were 3.4 (95% CI: 1.3–5.3) months and 5.2 (95% CI, 2.4–6.8) months, respectively. Eleven patients (36.7%) were previously treated with gemcitabine monotherapy and received this combination chemotherapy as a second-line treatment. Nineteen patients (63.3%) had previously undergone monotherapy or combination chemotherapy containing gemcitabine, S-1, and/or irinotecan and received this combination chemotherapy as a third- or fourth-line treatment. TTP was significantly longer in patients without history of S-1 use (5.6 versus 2.8 months; P=0.005). The relative dose intensity of S-1 and Ox was 89.0 and 96.7% of the scheduled dose, respectively. Major grade 3/4 adverse events included neutropenia (10.0%), anemia (3.3%), and diarrhea (6.7%). Peripheral neuropathy (limited to grade1/2) was observed in 43.3% of patients. There were no treatment-related deaths.

Conclusions: Combination chemotherapy with S-1 and Ox was moderately effective and well-tolerated in patients with refractory pancreatic cancer.

Purpose: To evaluate the efficacy and safety of chemotherapy for unresectable stage IVb pancreatic cancer.

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Results: The response rate and disease control rate was 2.8 and 47.2% in GEM monotherapy, 12.5 and 50% in S1 monotherapy, and 50 and 50% in GEM/S1 therapy, respectively. MST was 8.4 months in GEM monotherapy, 7.8 months in S1 monotherapy, 4.0 months in GEM/S1 therapy, and there were no significant differences among these three therapies. Grade 3 toxicities were observed in GEM monotherapy (neuropathy, seven patients; neutropenia, five patients; thrombocytopenia, one patient) and in GEM/S1 therapy (neutropenia, one patient; appetite loss, one patient).

Conclusion: Although each regimen was safe and yielded the high disease control rate for stage IVb pancreatic cancer, further evaluation how to choose the regimen as a first-line therapy is needed.
Poster Session 42: Gynecologic cancer

LATE RECURRENTCE OF MALIGNANT MELANOMA MIMICKING PRIMARY PERITONEAL CANCER

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Background: Malignant melanoma is an extremely malignant tumor with an unpredictable profile of spread and variable periods of remission. The late recurrence of malignant melanoma after diagnosis and treatment is a rare but characteristic metastatic behavior of malignant melanoma. When the late recurrence of malignant melanoma occurs, the most common sites of metastasis are the skin, subcutaneous tissues and lymph nodes.

Case: A 41-year-old woman presented with recurrent malignant melanoma which had clinical features of an acute state mimicking peritoneal cancer. Seven years after the excision of the primary tumor, the patient noticed diffuse abdominal distention. The patient underwent computed tomography and magnetic resonance imaging, which demonstrated extensive nodularity of the peritoneal surfaces, soft tissue thickening of the omentum and large amount of ascites. Therefore, primary peritoneal cancer was initially considered the most likely diagnosis. The patient underwent an exploratory laparotomy. Macroscopically, a numerous number of white-yellow rubbery nodules of tumor were present diffusely in the ovaries and omentum and on the uterine serosal surface. The pathological examination showed poorly differentiated adenocarcinoma of peritoneum. The tumor cells showed strong positivity by immunohistochemistry for S-100, melan A and vimentin. The diagnosis was established post-operatively by immunohistochemistry. Our case was an unusual recurrent case of malignant melanoma occurring 7 years after diagnosis and treatment of malignant melanoma.

Conclusion: The incidence of malignant melanoma has been increasing. The late recurrence of malignant melanoma may be seen frequently in the future. A variety of imaging and pathological methods including an exploratory laparotomy may be necessary in cases of patients suspecting peritoneal cancer with a previous history of melanoma.

TREATMENT PATTERNS AND PROGNOSIS OF FIGO STAGE IVB CERVICAL CANCER

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Objective: To assess treatment patterns and outcomes in patients with stage IVb cervical cancer.

Methods: A retrospective study of patients with stage IVb cervical cancer at a single institution was carried out.

Results: We identified 47 patients. The median progression-free survival and the overall survival were 5.7 and 11.1 months. Sixteen patients were treated with radiation therapy alone and 31 patients were treated with a combination of radiation therapy and chemotherapy. Of 45 recurrences or progression of disease, 25 patients received the best supportive care (BSC) and 20 patients received chemoradiotherapy or chemotherapy as an additional salvage treatment. The median overall survival was 11.1 months. The median progression-free survival was 5.7 months.

Conclusion: Non-chemotherapy, non-chemotherapy or non-radiotherapy after progression of disease and non-SCC histology were independent prognostic factors of survival.

A FUR ADVANCED GASTRIC CANCER CASES THAT ADJUSTING SUPPORTIVE CARE COULD IMPROVE QUALITY OF LIFE (QOL) AND RESTART SYSTEMIC CHEMOTHERAPY

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The case is 59-year-old male. He was received distal gastrectomy for locally advanced gastric carcinoma 6 months ago at other cancer center S-1/CDDP and was pointed multiple liver metastases, ascites and peritoneal disseminations out after 2 months. Therefore, he had carried out systemic chemotherapy combined oral fluorouracil with oxaliplatin (S-1/CDP regimen). After two cycles, because therapeutic response based on RECIST criteria was progression disease, he started second-line chemotherapy by weekly taxol regimen. Two days after, he visited to our hospital, as to bad performance status (PS). At that time, his PS was ECOG-PS 3, Kojima-PS 50, and his chief complaints were anorexia, severe general fatigue, severe abdominal pain, high-grade fever, drowsy and leg edema. We recognized them as secondary tumorous events by blood examination, urinal examination, CT scan and physical examination and recommended emergency admission to him. Directly, we stopped systemic chemotherapy and started variable supportive care, for example, pain control, secondary infection control, fever control, mental care (drug and counter), and his PS improved greatly (1 day after was 2, 6 days after was 1, 7 days after was 0). Sixteen days after, we could restart second-line chemotherapy by weekly taxol regimen and continue now. He is alive (PS 0) and can receive systemic chemotherapy at our hospital as outpatient. In this case, we recognized the fact is adjusting supportive care for cancer patient is very important to keep both patient quality of life and cancer therapy.

Poster Session 43: Palliative and supportive care case 1

NEUMOCYSTIS PNEUMONIA IN PATIENTS WITH SOLID TUMORS DURING CHEMOTHERAPY

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Background: Neumycystis pneumonia (PCP) is an opportunistic infection well recognized in patients with profound T cell immunodeficiency, especially in patients with AIDS. This infection is also a life-threatening complication seen during immunossuppressive chemotherapy for cancer or organ transplantation, so it is important to make an early diagnosis and start treatment. We present three cases of PCP developing during chemotherapy for solid malignancies.

Case reports: Case 1: A 50-year-old female received a first-line chemotherapy of gemcitabine–docetaxel (GT therapy) for leiomyosarcoma. After three cycles of GT therapy, she was admitted for a non-productive cough and high fever. Her chest radiograph and CT showed diffuse ground-glass bilateral opacities. SpO2 was 90% (room air). Serum β-D-glucan was 66.7 pg/ml. PCR of PCP by using BAL specimens was positive. We diagnosed PCP infection on the basis of these findings. Case 2: A 70-year-old female received gemcitabine (GEM) monotherapy as a first-line treatment of a pancreas cancer. After two cycles of GEM therapy, she developed dyspnea and a fever of 38°C. Her chest radiograph and CT showed diffuse ground-glass bilateral opacities. SpO2 was 92% (room air). Serum β-D-glucan was 40.8 pg/ml. We diagnosed PCP infection on the basis of these findings. Case 3: A 64-year-old female received neo-adjuvant chemotherapy with 5-fluorouracide, epirubicin and cyclophosphamide (FEC therapy) for breast cancer. After two cycles of FEC therapy, she was admitted for febrile neutropenia. Although the metastasis was recovered, she developed exertional dyspnea and a non-productive cough with continuous high fever. Her chest CT showed diffuse ground-glass bilateral opacities. SpO2 was 90% (room air). Serum β-D-glucan was 39.5 pg/ml. We diagnosed PCP infection on the basis of these findings.

Conclusion: We should be careful of not only drug-induced interstitial pneumonia and febrile neutropenia but also PCP during chemotherapy for solid malignancies.

SUCCESSFUL READMINISTRATION WITH OXALIPLATIN IN PATIENTS WITH ALLERGY TO OXALIPLATIN IN COLORECTAL CANCER PATIENTS

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Background: Oxaliplatin is an important drug of the treatment of colorectal cancer. It is known that some patients exhibit to be allergic to oxaliplatin during repeated treatment. As a result, administration of oxaliplatin is forced to be discontinued while there is a therapeutic effect. We report four patients successfully continued with oxaliplatin containing regimen after development of allergic symptom to the same drug by changing the method of drug administration.

Methods: Thirty-seven colorectal cancer patients were treated with an oxaliplatin containing regimen between October 2011 and December 2011. Four patients allergic to oxaliplatin received allergy treatment protocol. The allergy treatment protocol in mFOLOX6 regimen is different from the usual treatment protocol in following points: premedication with dexamethasone 13.2 mg IV, diphenhydramine 50 mg PO and famotidine 20 mg IV before oxaliplatin and oxaliplatin infusion in 4 h in the allergy treatment protocol (premedication with dexamethasone 6.6 mg IV, unpretreated with diphenhydramine and famotidine and oxaliplatin infusion in 2 h in the usual treatment protocol).

Results: Four patients allergic to oxaliplatin in the usual treatment protocol avoided the allergy after oxaliplatin readministration by the use of the allergy treatment protocol.

Conclusions: The allergy treatment protocol in mFOLOX6 regimen is effective in colorectal cancer patients allergic to oxaliplatin.
Poster Session 44: Palliative and supportive care case 2

P2 – 135
Severe cardiotoxicity in a patient with renal cell carcinoma treated with mTOR inhibitor: A case report

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Cardiotoxicity is an emerging concern with a new class of drugs known as targeted agents. Everolimus (afinitor) is the oral inhibitor of mTOR for the treatment of patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib. One of the most common laboratory abnormalities is hyperglycemia, which is reported in 7.7% patients receiving everolimus. We describe a 76-year-old man who was treated with everolimus for RCC with metastasis. The baseline echocardiogram was considered normal, and hBA1c was 5.7%. After 9 months of everolimus therapy, an echocardiogram revealed generalized left ventricular (LV) hypokinesia and severe LV dysfunction with ejection fraction of 42%, and his hBA1c increased from 5.7 to 9.8%. He started on insulin therapy for diabetes, besides everolimus therapy for RCC. Within 1 month, his LV ejection fraction increased from 42 to 57%. Careful monitoring of cardiac function and appropriate treatments for diabetes are required to recover cardiac dysfunction in a patient with RCC treated with everolimus.

Poster Session 45: Outpatient chemotherapy 3

P2 – 144
How should we manage the central vein access port system in outpatient cancer chemotherapy when the port system can be flushed, but no blood aspirated?

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Background: There are no reported data on the management of the central vein access port (CV-port) system when the CV-port system can be flushed, but no blood aspirated, mainly because a small thrombus occludes the catheter tip (catheter tip thrombosis). Moreover, it remains unclear whether catheter tip thrombosis needs to be treated.

Methods: From April 2008 to January 2012, 199 patients who were treated with outpatient chemotherapy via a CV-port in the Center for Clinical Oncology, Okayama University Hospital, were analyzed retrospectively.

Results: Of the patients, no blood could be aspirated in 21 (17.6%) when treated via a CV-port. The median time between CV-port placement and the failure of blood aspiration was 273 (range 7–1641) days. Among the patients with no blood aspiration from their CV-port, thirteen cases (61.9 %) had no complications other than failure of blood aspiration, and anticancer agents have been successfully administered. However, the other eight patients had their CV-port system replaced due to complications, including three catheter ruptures, two thrombotic events around the catheter, two infections, and one occlusion due to catheter bending.

Conclusions: Approximately 60% of patients might not require any treatment or intervention for the failure of blood aspiration from their CV-port. Medical staffs, however, should be aware that approximately one-third of the cases with no blood aspiration potentially have troubles with their CV-ports that need to be replaced.

Poster Session 46: Patient support

P2 – 152
Attitudes regarding informing clinical study result to participants in Japan

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Background: Informing the participants about study result is increased demand in recent years. Some studies reported that almost all participants want to receive study result. How much information do participants want and how do researcher offer were not mentioned. Moreover, there were concerned about resource for providing study result and the attitude regarding informing result to participants in Japan was not studied. The purpose of this study was aimed to discuss and propose the way of informing study results to Japanese participants.

Methods: Summarizing study result and a self-administrated questionnaire survey were conducted. Summary was created from abstract of academic paper with lay language and illustration using color. Objective study was oral uracil and tegafur compared with classic cyclophosphamide, methotrexate, fluorouracil as post-operative chemotherapy in patients with node-negative, high-risk breast cancer (NSAS-BC01 trial (J Clin Oncol 2009). Objective subject was participants of NSAS-BC01 trial in National Cancer Center Hospital.

Results: Summary of result was made a A4 format 4sheet. Fifty-eight patients responded to questionnaire of 116 patients (50%). In 58 responders, 92% of them preferred to be informed of the result. About 80% of responders answered that summary was clear to understand and 30% of them reported that the document should contain more information. The way of receive result preferred by the mail. When the result included bad news, 67% of responders wanted to receive result.

Conclusions: These answers suggested that participants in Japan desired to inform study result. Therefore, clinical study result should be provided participants whenever it takes time to get results, including bad news in a careful way. Summary of result should be created using lay language and illustration. Planning the cost, keeping participant contact list, and noticing participants that study result would be informed should be considered at the start of the study.

Poster Session 47: Malignant lymphoma 2

P2 – 158
Autologous stem cell transplantation for higher-risk diffuse large B-cell lymphoma in the first remission

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Background: Since significance of up-front autologous stem cell transplantation (ASCT) for aggressive lymphoma has not been established, we retrospectively analyzed the outcome of ASCT for higher risk diffuse large B-cell lymphoma (DLBL) in the first remission.

Patients and methods: Among 61 patients with DLBL classified as high or high-intermediate risk using international prognostic index, ASCT was carried out in 37 patients in the first remission induced by CHOP regimen. They consist of 22 male and 15 female. Their median age was 66.5 (range 23–73). Stem cells were mobilized by etoposide and conditioning regimen consisted of ranimustine, carboplatin,
etoposide, and cyclophosphamide. Rituximab was used in 11 patients. The survival outcome of ASCT was compared with that of 10 patients who rejected ASCT.

**Results:**

1. The outcome of ASCT was compared with that of 10 patients who rejected ASCT.
2. In 31 (male:female 14:17; median age 60 (23–80)) patients the diagnosis of hematological malignancy was confirmed by image-guided needle biopsy of non-superficial lymphadenopathy/mass lesions.

**Discussion:**

- The clinical characteristics of cases in which the diagnosis of hematological malignancies was confirmed by image-guided needle biopsy of non-superficial lymphadenopathy/mass lesions.
- Method: A retrospective chart review was carried out to identify patients who were suspected as having hematological malignancies by intra-abdominal or thoracic lymphadenopathy/mass but lack superficial lymphadenopathy/subcutaneous mass, and underwent image-guided needle biopsy to confirm the diagnosis.
- Results: In 31 (male:female 14:17; median age 60 (23–80)) patients the diagnosis of hematological malignancy was confirmed. 26 biopsies were guided by CT, and 5 by US. No major adverse events were observed. Biopsy sites varied including retroperitoneum (17), mesentry (9), mediastinum (3), pleural cavity (1), and lung (1). Follicular lymphoma (FL) was the most frequent diagnosis, followed by diffuse large B cell lymphoma (39%), adult T cell leukemia/lymphoma (7%), and plasmacytoma (3%). FL accounted for 68.8% of cases presented with retroperitoneal lymphadenopathy/mass alone. Of note, these FL cases tended to be on early stage, but there are no other clinical characteristics; such as the proportion of the cases with bone marrow invasion and the SUV level in PET scans.

**Discussion:** FL was the most prevalent among cases with retroperitoneal lymphadenopathy/mass. Considering that FL constitutes 7–15% of all lymphomas in Japan, our findings suggest that FL more commonly presents at retroperitoneal sites without evident superficial lymphadenopathy.

**Poster Session 50: Brain tumor**

**P3 – 001**

**IDENTIFICATION AND VALIDATION OF A GENE EXPRESSION SIGNATURE THAT PREDICTS THE OUTCOME IN MALIGNANT GLIOMA PATIENTS**

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Better understanding of the underlying biology of malignant gliomas is critical for the development of early detection strategies and new therapeutics. This study aimed to define genes associated with survival. We investigated whether genes selected to define subgroups of gliomas objectively. RNAs from 50 non-treated gliomas were analyzed using the GeneChip Human Genome U133 Plus 2.0 Expression array. We identified 82 genes whose expression was strongly and consistently related to patientsurvival. For practical purposes, a 15-gene set was also selected. Both the complete 82 gene signature and the 15 gene set subgroup indicated their significant predictivity in the three of four independent external data set (total n = 565). Our method was effective for objectively classifying gliomas, and provided a more accurate predictor of prognosis. We assessed the relationship between gene expression and outcome by using the random survival forests model and this performance was a better classifier compared with significance analysis of microarrays.
Poster Session 51: Head and neck cancer

A PROSPECTIVE MULTICENTER PHASE II STUDY OF CISPLATIN AND WEEKLY DOCETAXEL AS FIRST-LINE TREATMENT OF RECURRENT OR METASTATIC NASOPHARYNGEAL CANCER (KCGS HN07-01)

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Background: The purpose of this phase II study was to determine the efficacy and toxicity of cisplatin and weekly docetaxel combination chemotherapy as a first-line treatment in patients with recurrent or metastatic nasopharyngeal cancer.

Methods: Recurrent or metastatic nasopharyngeal cancer patients were enrolled and received a combination of weekly docetaxel (35 mg/m\(^2\) on days 1 and 8) and cisplatin (70 mg/m\(^2\) on days 1 and 8) every 21 days, for up to a maximum of six cycles. The primary end point was the objective response rate, and the secondary end points included the toxicity of combination chemotherapy, progression-free survival, overall survival and 1-year survival rate. The study is registered with ClinicalTrials.gov, number NCT01312311.

Results: In total, 47 patients were enrolled and analyzed and 46 patients (97.9%) completed the planned protocol. In an intent-to-treat analysis, 6 patients (12.8%) achieved complete response and 27 patients (57.4%) showed partial response, with an objective response rate of 70.2%. The median progression-free survival and overall survival were 9.6 months (95% CI: 5.7–13.5 months) and 28.5 months (95% CI: 16.9–40.1 months), respectively, and the 1-year survival rate was 89.9%. The common grade 3 adverse events were stomatitis (1.2%), neutropenia (0.8%), anemia (0.8%), infection (0.8%) and diarrhea (0.8%). Grade 4 adverse events were not observed in this study.

Conclusions: The combination chemotherapy of cisplatin and weekly docetaxel is highly effective and shows favorable toxicity as a first-line chemotherapy in patients with recurrent or metastatic nasopharyngeal cancer.

Poster Session 52: Clinical pharmacology

EVALUATION OF THE FORMULA DEVELOPED BY THE JAPAN SOCIETY OF NEPHROLOGY FOR ESTIMATING RENAL FUNCTION OF PATIENTS WITH LUNG CANCER TREATED WITH CARBOPLATIN CONTAINING CHEMOTHERAPY

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Background: The Calvert formula is routinely applied for the dosing of carboplatin based on glomerular filtration rate (GFR) as accurately measured using the 51-Cr-EDTA clearance. In general practice, an estimated value of creatinine clearance calculated by the Cockcroft-Gault formula is widely used as a substitution of the GFR. It is reported that there is ethnic difference in renal function and that decrease of GFR by aging is less in Japanese than Caucasians. In 2008, the project of the Japan Society of Nephrology developed the following formula for the calculation of GFR fitting to Japanese patients: GFR (ml/min/1.73 m\(^2\)) = 194 x serum creatinine\(^1.046\) x age\(^-0.194\) (in Japanese female) or GFR (ml/min/1.73 m\(^2\)) = 199 x serum creatinine\(^1.026\) x age\(^-0.211\) (in Japanese male). We aimed to evaluate the efficacy of this new estimated method of renal function for Japanese patients with lung cancer. Consecutive patients treated with carboplatin containing chemotherapy were examined. Dosage of carboplatin was determined by the Calvert formula with a target AUC of 5 and GFR calculated by the equation described above. Relationships between adverse effects and clinical features were analyzed.

Results: A total of 34 patients (22 males/12 females) were included. Fifteen of the patients received carboplatin/gemcitabine, six received carboplatin/paclitaxel, one received carboplatin/docetaxel and seven received carboplatin/pemetrexed. The mean count of neutrophilcyte and platelet at nadir were 1377 ± 1160 and 12.3 ± 6.8 × 10\(^4\)/\(\mu\)l, respectively. One patient experienced severe thrombocytopenia requiring a blood transfusion; however, the hematological toxicities of the others were mild. There were no correlations between hematological toxicity and clinical values including renal function, age, sex and body surface area.

Conclusion: The newly developed formula is effective compensating for inter-patient variability including age, sex and renal function in Japanese patients treated with carboplatin. Ethnic differences including renal function should be taken into consideration for personalized dosing.

TRASTUZUMAB-BASED THERAPY FOR METASTATIC SALIVARY DUCT CARCINOMA OVER-EXPRESSING HER2: CASE REPORT OF A COMPLETE RESPONSE

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Background: Salivary duct carcinoma (SDC) is an aggressive tumor with high mortality. Except surgical operation and radiotherapy, there is no consensus on the role of optimal treatment. Histopathologically, SDC is morphologically similar to invasive breast carcinoma, and over-expression for HER2 has been also reported in recent years.

Case: We present a 35 years-old woman diagnosed with introral SDC in the maxillary gingiva. Eight months after completion of surgery and adjuvant radiotherapy, she developed local recurrence. In spite of additional surgery, CyberKnife radiosurgery, proton beam therapy, and chemotheray (5-fluorouracil) as alternative therapy, she developed multiple metastases and a massive local recurrence. Since she had been resistance to various treatment, the excised specimen has been evaluated again. Immunohistochemistry analysis showed strong (3+) overexpression for HER2.

Result: After institutional review board and cancer board approved consents of off-label, she received concomitant chemotherapy with trastuzumab (8 mg/kg dose-loading and 6 mg/kg) and docetaxel (75 mg/m\(^2\)) every 21 days. The tumor was reduced quickly and complete clinical response was attained seven months after treatment initialized.

Conclusions: SDC is uncommon in the salivary gland neoplasm and there are limited data because of their rarity. As histologically resembled, SDC appears to be strongly overexpress HER2 at much higher frequency than breast carcinoma. We treated a very rare case of SDC with trastuzumab and attained a complete clinical response. Trastuzumab-based therapy might be an effective regimen for advanced SDC over-expressing HER2. Recently, trastuzumab plus chemotherapy also improved survival in patients with HER2 positive gastric cancer compared with chemotherapy alone. In view of validity having been shown also in the HER2 positive gastric cancer and moreover breast cancer, drug development might be advanced to biomarker oriented from now on regardless the kind of cancer.

QUALITY OF LIFE IN ELDERLY PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY FOR NON-SMALL-CELL LUNG CANCER: PROSPECTIVE COMPARISON STUDY


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Introduction: The incidence of lung cancer increases with age. Given the increasing comorbid conditions and progressive reduction of organ function, it is presumed that the elderly are less likely to tolerate to the cytotoxic chemotherapy. However, prospective data on adjuvant chemotherapy in elderly patients are not available.

Methods: Patients with completely resected stage Ib, II or IIA NSCLC were enrolled for this analysis. Either four cycles of paclitaxel–carboplatin or vinorelbine–cisplatin was used as an adjuvant chemotherapeutic regimen. The primary objective was to assess the health-related quality of life (HRQOL) of elderly patients (age ≥65) during and after post-operative chemotherapy. The secondary objective included comparison of HRQOL by age (≥65 versus <65). For the assessment of HRQOL, EORTC QLQ-C30 and EORTC QLQ-LC13 were used. For statistical analysis, generalized estimating equations (GEE) was used.

Results: Between October 2008 and October 2011, a total of 113 patients were enrolled; aged ≥65 (n = 60, 53.1%), aged <65 (n = 53, 46.9%). Baseline characteristics including gender, clinical stage, type of surgery, chemotherapeutic regimen were not significantly different between ≥65 and <65. EORTC QLQ-C30 and EORTC QLQ-LC13 were used. For statistical analysis, generalized estimating equations (GEE) was used.
Conclusions: Post-operative chemotherapy did not substantially reduced HRQOL in elderly NSCLC patients, and HRQOL during and after adjuvant chemotherapy did not differ by age (<65 versus ≥65).

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Background: Thymic epithelial tumors (TETs), thymoma and thymic carcinoma, are the most common tumor of the anterior mediastinum. Initial complete resection is the most powerful prognostic indicator of survival. However, it is obviously related to stage. Here, we report the result of a prospective phase II study of neoadjuvant docetaxel/cisplatin in patients with locally advanced TETs.

Methods: In this open-label, phase II, non-randomized study, patients with histologically proven, masaoka stage III/IV TETs at presentation were enrolled. Patients received docetaxel 75 mg/m2 I.V for 1 h, followed by I.V cisplatin 75 mg/m2 over 1.5 h on day 1 of every 3 week. After 3 cycles of chemotherapy, subsequent surgery was carried out, if resectable.

Results: From March 2007 to July 2011, a total of 27 TETs patients were entered into the trial. The median age was 54 (range, 15–68), and Masaoka stage at presentation was III (n = 8, 29.6%), IVa (n = 17, 63.0%), and IVb (n = 2, 7.4%). Histologic type by the WHO includes type B1 (n = 16, 59.3%), B2 (n = 0.27). P3 – 017

A PROSPECTIVE, PHASE II TRIAL OF INDUCTION CHEMOTHERAPY WITH DOCETAXEL/CISPLATIN FOR MASAOKA STAGE III/IV THYMIC EPITHELIAL TUMORS

P3 – 018

CONCOMITANT POLYPHARMACY IS ASSOCIATED WITH IRINOTECAN-INDUCED ADVERSE DRUG REACTIONS IN PATIENTS WITH CANCER

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Background: Patients with cancer are often given chemotherapeutic agents concurrently with other medications to treat comorbidity. The practical effects of concomitant medications, especially polypharmacy, on adverse drug reactions induced by irinotecan-based chemotherapy were not well documented.

Methods: Associations of adverse drug reactions related to irinotecan monotherapy or a combination of irinotecan, 5-fluorouracil, and l-leucovorin (FOLFIRI) with concomitant medications used to treat comorbidity were retrospectively investigated in Japanese patients with cancer. Concomitant medications were defined as therapeutic drugs which were given to manage comorbid conditions besides cancer, and those continuously administered at least from the last visit before the start of irinotecan-based chemotherapy until after day 1 of the chemotherapy.

Results: Among the 172 patients, 118 received concomitant medications. Almost all concomitant medications were prescribed from the last visit before starting irinotecan-containing chemotherapy to until the end of the first cycle. Twenty one patients had grade 4 neutropenia and/or grade 3 or 4 diarrhea.

Univariate and multivariate analyses revealed that concomitant medications were significantly associated with irinotecan-related severe neutropenia and/or diarrhea (P = 0.023 and 0.044). Multiple concomitant medications were significantly related to severe irinotecan-related toxicity in patients given monotherapy or FOLFIRI (P = 0.01). The incidence of severe irinotecan-related toxicities increased in parallel to the number of concomitant medications.

Conclusion: We thus demonstrated that multiple concomitant medications were significantly associated with irinotecan-related severe toxicity in patients with cancer who received irinotecan-based chemotherapy, indicating that polypharmacy must be effectively managed to decrease the risk of adverse drug reactions.

P3 – 020

STATISTICAL EXAMINATION TO DETERMINE WHETHER ONLY 48-H VALUE FOR SERUM CONCENTRATION DURING HIGH-DOSE METHOTREXATE THERAPY IS A PREDICTOR FOR CLINICAL ADVERSE EVENTS USING ORDERED LOGISTIC REGRESSION ANALYSIS

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Sustained elevation of serum methotrexate (MTX) concentrations (>1.0 µM) for 48 h (48-h value) has been found to have predictive significance for the development of toxicity. However, we sometimes experience severe adverse events during high dose (HD)-MTX therapy even if serum MTX concentrations comply with recommended values. We carried out a retrospective study to identify predictors for occurrence of adverse events, and examined whether only 48-h value is a statistically significant predictor for clinical adverse events during HD-MTX therapy. The subjects were 32 hematological patients (n = 58 episodes) treated with MTX at Kyoto Prefectural University of Medicine between February 2003 and July 2007. Ordered logistic regression analysis was used to identify predictors for occurrence of adverse events. The predictive factors identified were:24-h continuous infusion therapy (24-h C-IV) (long infusion time) [odds ratio (OR) = 2.890, CI = 1.493–5.594; P = 0.0016] for fatigur, higher dose (OR = 2.282, CI = 1.267–4.046; P = 0.0048) and combination chemotherapy (OR = 2.177, CI = 1.059–4.477; P = 0.0344) for stomatitis, and 24 h C-IV (OR = 2.573, CI = 1.101–6.016; P = 0.0294) for neutropenia. We found that only the 48-h value was not a predictor for clinical adverse events for HD-MTX therapy. A major limitation of the present study was the small number of participants. However, our findings suggest there is evidence that a long infusion time is a significant predictor for general fatigue and neutropenia, while a higher dose and combination chemotherapy are predictors for stomatitis. (Kanbayashi Y, et al. Ann Hematol. 2010; 89: 965–9.)

Poster Session 53: Lung cancer bone metastasis

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Background: The bone resorption biomarker sNtX has been previously shown to add value as an aid in the diagnosis of bone metastasis in patients with lung cancer. The objective of this prospective study was to determine whether periodic sNtX measurements could lead to early diagnosis of bone metastasis in patients with lung cancer.

Methods: Patients with newly diagnosed organ-confined lung cancer were enrolled. sNtX values were determined once each month using the OSTEOMARKSTM serum NTX assay (Alere Medical). The presence or absence of bone metastasis was determined by monthly physical examination and by bone scintigraphy every 3 months for 12 months. All patients were required to provide written informed consent.

Results: Forty patients were enrolled between June and December 2010. One patient withdrew early and was excluded from analysis. The mean ± SD baseline level of sNtX was 17.5 ± 4.4 nM BCE/L. Five patients developed bone metastasis (as characterized by bone scintigraphy) during the study period. The level of sNtX in subjects with bone metastasis was slightly increased (21.6 ± 3.2 nM BCE/L), however, in these patients, there was no statistically significant difference between NTX values at baseline (18.2 ± 4.2 nM BCE/L) and when metastasis was diagnosed. (P = 0.176).

When a cut-off value of sNtX was set to 22.0 nM BCE/L, the sensitivity and the
specify of detection of bone metastasis were 80.0% and 42.1%, respectively. Using this cut-off, the elevation of sNTx could predict bone metastasis at least one month before diagnosis. Bone scintigraphy in all 5 patients, however, the specificity was relatively low for clinical implementation. Additionally, the sensitivity and the specificity of early detection of systemic spread of disease (including bone metastasis) were 70.6% and 45.5%, respectively.

Conclusions: Periodic determination of sNTx in patients with organ confined lung cancer did not provide sufficient specificity for it to be used for the early diagnosis of bone metastasis or disease progression.

USEFULNESS OF SERIAL MEASUREMENT OF SERUM N-TELOPEPTIDES OF TYPE I COLLAGEN (NTX) IN PATIENTS WITH LUNG CANCER WHO DEVELOPED BONE METASTASIS: A PROSPECTIVE STUDY

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Background: The bone resorption biomarkers urinary NTx (uNTx) and serum NTx (sNTx) have been shown to aid in the diagnosis of bone metastasis in patients with lung cancer. Patients with metastatic bone disease (MBDLC) are often treated with zoledronic acid. Zoledronic acid reduces the levels of bone resorption biomarkers and also the risk of skeletal adverse events in patients with MBDLC.

We studied the effects of treatments including zoledronic acid on levels of sNTx during disease progression.

Methods: Patients with MBDLC at the initial diagnosis were entered to this study. sNTx was measured once a month using the sNTx assay OSTEOMARKTM serum NTx (Alere Medical). MBDLC was characterized by monthly physical examination and bone scintigraphy every 3 months for 12 months. All patients were required to provide written informed consent.

Results: Twenty patients were enrolled between June and December 2010. The mean ± SD of the sNTx concentrations was 19.8 ± 5.8 nM BCE/L at baseline. In the 16 patients receiving zoledronic acid, the levels of sNTx showed a significant decrease in the first month of treatment (baseline: 21.3 ± 5.5 nM BCE/L; one month later: 13.6 ± 2.7 nM BCE/L; P < 0.01). During follow-up period, 12 of the patients treated with zoledronic acid experienced worsening MBDLC or had died from lung cancer, and there were statistically significant differences in the levels of sNTx at baseline (19.7 ± 4.47 nM BCE/L) at the lowest levels after the administration of zoledronic acid (11.5 ± 2.73 nM BCE/L) and at the point of measurable disease progression or death (13.0 ± 2.07 nM BCE/L).

Conclusions: Serial measurements of sNTx in patients with MBDLC treated with zoledronic acid might predict disease progression of bone metastasis. Administration of zoledronic acid significantly decreased the level of sNTx from baseline within one month and maintained the level of sNTx lower than baseline during study periods.

THE CLINICAL SIGNIFICANCE OF THE SERUM CROSS-LINKED N-TELOPEPTIDE OF TYPE I COLLAGEN AS A PROGNOSTIC MARKER FOR NON-SMALL-CELL LUNG CANCER

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Lung cancer is the leading cause of cancer-related death. Many patients with lung cancer are in the advanced stages of the disease at the time of diagnosis. The 5-year survival rate for lung cancer was 10-20%, and the prognosis of lung cancer is still poor. The cross-linked N-terminal telopeptide of type I collagen (NTx) is a metabolite of type I collagen, the main constituent of the bone matrix. We measured serum NTx who underwent staging during hospitalization for initial treatment of lung cancer in our department. Then, we examined whether serum NTx would be relevant to the prognosis of non-small-cell lung cancer. This study included 176 lung cancer patients (125 males and 51 females), including 109 adenocarcinoma, 53 squamous cell carcinoma, 6 large cell carcinoma, and 8 other cancer types. Univariate and multivariate analysis with the Cox proportional hazards model revealed that a particularly close association was found between gender, PS, disease stage, and serum NTx level and OS. Especially, a median OS of 368 days was observed for patients with a serum NTx level of <22 nmol BCE/L, which was significantly longer than the 197 days observed for patients with a serum NTx level of ≥22 nmol BCE/L (hazard ratio, 2.02; 95% confidence interval, 1.36-2.99). Log-rank test showed that a high serum NTx level (>22 nmol BCE/L) appears to be a risk factor for a reduction in OS in patients with NSCLC.

THE SURVIVAL IMPACT OF THE SEVERITY OF NEUTROPENIA IN FRONTLINE CHEMOTHERAPY WITH CARBOPLATIN AND PaclitaxEL FOR ADVANCED NSCLC

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Background: The survival impact of neutropenia in chemotherapy for advanced NSCLC has been well discussed. We retrospectively analyzed the contribution of the severity of neutropenia to the survival of the patients who were treated with carboplatin and paclitaxel.

Methods: We retrospectively reviewed the medical records of all patients with NSCLC who were treated from January 1999 to December 2010 in Kansai Medical University Taki Hospital. Patients were included in this study if they had an advanced NSCLC (IIIb or IV) that was treated with front-line chemotherapy with carboplatin and paclitaxel.

Results: 402 patients of NSCLC were treated in our hospital during above period. One hundred and sixty-seven patients were met to the eligible criteria. The median age was 65 (31-79). Female and male were 42 and 125 respectively. Adenocarcinoma, squamous cell carcinoma, and large cell carcinoma were 118, 44 and 4, respectively. Grade 3/4, 1/2 and 0 neutropenia were observed in 55.7, 23.4 and 21.0%, respectively. The overall response rate of the groups of grade 3/4, 1/2, 0 neutropenia were 40.7, 38.1, and 21.9%, respectively. The MST for the patients of grade 3/4, 1/2 and 0 neutropenia were
Poster Session 55: Gastrointestinal cancer case 5

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Anti-EGFR antibody is effective for Kraś wild-type colorectal cancers (CRCs), but not effective for the Kraś mutation-type. Recently, some reports have shown that it is effective for Kraś G13D mutation-type CRCs. Herein, we reported two cases of Kraś G13D mutation-type CRCs treated by anti-EGFR antibody with sufficient explanation and informed consent. Case 1: A 66-year-old female patient underwent left colectomy for descending colon cancer in January 2009. The clinical stage was IIB. Although adjuvant chemotherapy was given, metastasis to para-aortic lymph nodes occurred in January 2010. After four cycles of Xeloda + bevacizumab and 17 cycles of FOLFIRI, the recurrent tumors showed progression in July 2011. The primary tumor had Kraś G13D mutation. Therefore, four cycles of Panitumumab administration was conducted. The serum level of CEA was decreased (from 45.5 to 18.9), and no deterioration of para-aortic lymph node metastasis was seen. However, new lesions of lung metastasis and hydrothorax occurred, and chemotherapy was stopped. Case 2: A 62-year-old female patient underwent transverse colecctomy and total hysterectomy + bilateralsalpingo-oophorectomy for transverse colon cancer and ovarian metastases in March 2009. Clinical stage was IV. Eight cycles of FOLFIRI followed by four courses of FU/LV and capecitabine monotherapy were given as adjuvant chemotherapy. In August 2010, peritoneal dissemination and lung metastasis were detected. After 14 cycles of FOLFIRI + Bevacizumab, the recurrent tumors showed progression. The primary tumor had Kraś G13D mutation; therefore, four cycles of Panitumumab administration was conducted. Although the serum levels of tumor markers were decreased (CEA: from 138.2 to 267.2, CA19-9: from 55.2 to 28.8), the lung metastasis showed progression, and chemotherapy was stopped. Although the evidence level is still limited, anti-EGFR antibody treatment may be an option in Kraś G13D mutation-type CRCs.

P3 – 047

NECROLYTIC MIGRATORY ERYTHEMA ASSOCIATED WITH PANCREATIC GLUCAGONOMA

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Glucagonoma, a rare tumor derived from the α-cells of the pancreas, has an estimated incidence of approximately one in 20 million people per year. This glucagonoma results in clinical manifestations including necrolytic migratory erythema (NME), chelitis, diabetes mellitus, anemia, weight loss, among others. Of these, NME is a well-known paraneoplastic symptom observed in patients with glucagonoma. However, NME is often missed at initial investigation, and the correct diagnosis of glucagonoma tends to be delayed. We report a 46-year-old Japanese woman with glucagonoma who presented with mucocutaneous manifestations 1 year before the diagnosis of the pancreatic neoplasm with multiple liver metastases. Contrast-enhanced dynamic CT of the abdomen revealed multiple tumors in the peritoneum, and caused lymph node metastasis in retroperitoneum and distant metastasis in the liver, both lungs, and pancreas. Pathological diagnosis was adenocarcinoma originating from the small intestine. Cancer of the small intestine is very rare as 1% or less of all the alimentary canal malignancy and this case with autopsy can provide precious clinical information for cancer of the small intestine. We hope to report this precious case with bibliographic consideration.

P3 – 048

AN AUTOPSY CASE OF PRIMARY ADENOCARCINOMA OF THE SMALL INTESTINE

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A 59-years-old male consulted our hospital for loss of appetite which was maintained more than half a year. Abdominal contrast enhanced CT showed intraperitoneal tumor whose diameter was up to 17 cm, whole body lymph node enlargement, and multiple tumors of the liver. Although the liver biopsy and the neck lymph node biopsy failed to lead confirmed pathological diagnosis, laparoscopic tumor biopsy revealed intraperitoneal tumor was pathologically adenocarcinoma. The primary origin was unknown but imaging inspection indicated the origin might be small intestine. The chemotherapy (FOLFIRI) was started according to standard regimen for advanced colorectal cancer. Although the tumor size was temporarily decreased to the diameter of 12 cm, it turned to be progressive two months afterward. The regimen was thus switched to FOLFIRI but the progression was unstoppable, caused acute renal failure, and persisted him four months after the FOLFIRI had started. The bereaved family’s consent was obtained and the autopsy was done 1 h after the death. The intraoperative tumor with a diameter of the maximum of 15 cm was located on the small intestine, infiltrated into the bladder and the rectum, disseminated to the peritoneum, and caused lymph node metastasis in retroperitoneum and distant metastasis in the liver, both lungs, and pancreas. Pathological diagnosis was adenocarcinoma originating from the small intestine. Cancer of the small intestine is very rare as 1% or less of all the alimentary canal malignancy and this case with autopsy can provide precious clinical information for cancer of the small intestine. We hope to report this precious case with bibliographic consideration.

Poster Session 56: Gastrointestinal cancer

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Background: Evidence-based data regarding the role of chemotherapy in the management of gastrointestinal neuroendocrine tumors are scarce, mainly because the results of only small studies are available. Combination chemotherapy with regimens such as cisplatin-etoposide was reported to have activity against gastrointestinal neuroendocrine tumors. However, few studies have documented a good response of gastrointestinal neuroendocrine tumors to second-line chemotherapy. Patients and methods: We studied three patients with unresectable gastrointestinal neuroendocrine tumors who received irinotecan or amrubicin after prior chemotherapy with platinum and etoposide. Results: The characteristics of the three patients are shown below. All were men, with a median age of 69 years (range, 62–70). The site of the primary tumor was the stomach and the esophagus in one. One patient with a gastric neuroendocrine tumor received irinotecan as second-line chemotherapy, and the other received amrubicin as second-line chemotherapy.
second-line chemotherapy followed by irinotecan as third-line therapy. A partial response was obtained in one patient after two courses of irinotecan, and this patient is now receiving the fifth course of irinotecan. The patient with an esophageal neuroendocrine tumor received amrubicin as second-line chemotherapy, followed by irinotecan as third-line therapy. The second course of irinotecan is now being administered, and response will be evaluated after completion of the second course. Both patients who received amrubicin as second-line therapy had progressive disease after two courses of amrubicin.

Conclusions: We described our experience with a case of gastrointestinal neuroendocrine tumor that responded to irinotecan after prior chemotherapy. Irinotecan might be effective against gastrointestinal neuroendocrine tumor. However, further clinical studies are required to confirm currently available evidence.

EVALUATION OF THE EFFICACY OF DOXORUBICIN THERAPY FOR PATIENTS WITH LOCALLY RECURRENT RECTAL CANCER

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Background: Doxorubicin is approved for the treatment of gastrointestinal cancer in Japan. However, the efficacy data are based on clinical trials carried out many years ago. Whether doxorubicin is effective against gastrointestinal cancer after current standard chemotherapy remains unknown.

Patients and methods: We evaluated the efficacy of doxorubicin in patients with gastrointestinal cancer who had previously received standard chemotherapy. Efficacy was evaluated according to the RECIST criteria.

Results: A total of 12 patients (11 men and 1 woman) had received doxorubicin. Their median age was 62 years (range, 40 to 78). The tumor types were colorectal cancer (5 patients), gastric cancer (4 patients), pancreatic cancer (2 patients), and hepatocellular carcinoma (1 patient). The response of colorectal cancer was CR/PD/SD/PD (0/0/5/5), and the median number of courses of doxorubicin was 1 (range, 1–2). The response of gastric cancer was (0/1/0/3), and the median number of courses of doxorubicin was 2 (range, 1–6). The response of pancreatic cancer was (0/1/1/0), and the median number of courses of doxorubicin was 6 (range, 5–7). The response of hepatocellular carcinoma was (0/0/1/0), and the number of courses of doxorubicin was 10.

Conclusions: One of the two patients with pancreatic cancer had a partial response to doxorubicin after previously receiving standard chemotherapy. Stable disease was obtained in the other patient with pancreatic cancer and one patient each with gastric cancer and hepatocellular carcinoma. No clinical benefit was obtained in colorectal cancer.
colorectal cancer at our institution between March of 2006 and August of 2011. As for impact of primary tumor resection on survival, we compared overall survival between resected and unresected patients and evaluated some predictive factors in the analysis of survival. In unresected patients, we evaluated incidence of primary tumor related complications and some predictive factors associated with the incidence of complications.

Results: Median follow-up period was 14.0 months. A total of 37 patients underwent resection of the primary tumor, whereas 40 patients were managed without resection. Patient characteristics were well-balanced between the two groups. Resected patients had significantly better median survival time compared with unresected patients (24.3 versus 14.0 months). Perioperative complications in resected patients were low in both frequency and severity, and the period from resection to either discharge or start of chemotherapy was not significantly extended. Univariable analysis identified three significant predictive factors of survival: location of primary tumor, number of distant metastasis, and ALP, and ALP was also a significant predictor of survival in a multivariable analysis. Incidence of primary tumor related complications was 25%, and univariable analysis identified no predictive factors.

Conclusions: Primary tumor resection in patients with incurable and asymptomatic stage IV colorectal cancer may be associated with better overall survival, and primary tumor related complications may be unavoidable to some extent in unresected patients. We plan to present the updated results with extended follow-up period at the presentation.

Poster Session 59: Pancreatic cancer 2

P3 – 075
GEMCITABINE PLUS RADIOTHERAPY IN PATIENTS WITH UNRESECTABLE LOCALLY ADVANCED PANCREATIC CANCER
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Background: Chemoradiotherapy is a treatment option for unresectable locally advanced pancreatic cancer. Loehrer et al. reported that gemcitabine plus radiotherapy (GEM-RT) improved overall survival compared with gemcitabine alone (J Clin Oncol 2011). The purpose of this study was to prospectively evaluate the efficacy and tolerability of GEM-RT in Japanese patients.

Methods: Patients with unresectable locally advanced pancreatic cancer without prior chemotherapy or radiotherapy were treated with GEM-RT, which comprised gemcitabine (600 mg/m2/week for weeks 1 to 5 with radiotherapy as induction therapy, then 1000 mg/m2/week for 3 of 4 weeks as consolidation therapy) plus radiation therapy (starting on day 1, total 50–50.4 Gy). Treatment was continued until disease progression, unacceptable toxicity, or patient refusal. The primary outcome measure was the response rate.

Results: From September 2008 to September 2011, 17 consecutive patients were enrolled in our hospital. The median age was 76 years. The rate of completing all planned cycles of gemcitabine and radiotherapy in the induction phase was 88% and 94%, respectively. Adverse events occurred in all patients. Hematologic and gastrointestinal toxicities were common. Five patients were affected with gastrointestinal ulcers. Grade 3 or 4 toxicities were observed in 16 patients; however, only two patients stopped GEM-RT because of adverse events. The objective response rate and disease control rate according to RECIST version 1.1 were 41 and 76%, respectively. The median progression-free survival was 10.9 months. The median survival time was 14.0 months.

Conclusions: GEM-RT is associated with many toxicities, but is generally manageable. GEM-RT may be an effective therapy for unresectable locally advanced pancreatic cancer.

P3 – 074
DACARBazine MONO-ThERAPY FOR UNRESECTABLE NEUROENDOCRine TUMOR: A RETROspective ANALYSIS
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Background: Complete resection has been the only potentially curative treatment of pancreatic cancer. Primary tumor resection in patients with incurable and asymptomatic stage IV colorectal cancer may be associated with better overall survival, and primary tumor related complications may be unavoidable to some extent in unresected patients. We plan to present the updated results with extended follow-up period at the presentation.

Results: Median follow-up period was 14.0 months. A total of 37 patients underwent resection of the primary tumor, whereas 40 patients were managed without resection. Patient characteristics were well-balanced between the two groups. Resected patients had significantly better median survival time compared with unresected patients (24.3 versus 14.0 months). Perioperative complications in resected patients were low in both frequency and severity, and the period from resection to either discharge or start of chemotherapy was not significantly extended. Univariable analysis identified three significant predictive factors of survival: location of primary tumor, number of distant metastasis, and ALP, and ALP was also a significant predictor of survival in a multivariable analysis. Incidence of primary tumor related complications was 25%, and univariable analysis identified no predictive factors.

Conclusions: Primary tumor resection in patients with incurable and asymptomatic stage IV colorectal cancer may be associated with better overall survival, and primary tumor related complications may be unavoidable to some extent in unresected patients. We plan to present the updated results with extended follow-up period at the presentation.

Poster Session 59: Pancreatic cancer 2

P3 – 075
PROGNOSIS OF ADENOSQUAMOUS CARCINOMA OF THE PANCREAS: A MATCHED CASE-CONTROL STUDY
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Background and aim: Adenosquamous carcinoma of the pancreas (ASC), account for only 1-4% of exocrine pancreatic malignancies, is one of the variants of pancreatic ductal adenocarcinomas (PDAC). However, the prognosis of ASC is still unclear since these reports were based on only case studies and small surgical series with early stage cancers. The purpose of our study was to clarify the prognosis of ASC using a matched case-control study.

Study design: We evaluated pathological and clinical records of ASC between 2001 and 2011 in our institution. All of ASC cases were diagnosed with either surgical specimen or endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). In order to clarify the prognosis of ASC, we evaluated clinical characteristics of ASC. As a control, PDAC cases matched with ASC cases for sex, age, pretreatment ECOG-F, location, initial treatment and the AJCC TNM staging for pancreatic cancer, were also included in this study.

Results: Of the 914 cases of the pancreatic neoplasms, 28 cases of ASC were identified (3.06%), and 56 cases of PDAC were matched to a control. Of 28 cases of ASC, 6 cases underwent curative resection and 22 cases were unresectable. Overall survival (OS) of ASC was significantly worse than that of PDAC with a hazard ratio (HR) of 1.94 (95% CI, 1.07 to 3.51; P = 0.026; median 8.38 months versus 15.75 months). Of the 22 unresected cases, OS of ASC was significantly worse than that of PDAC with a HR of 2.39 (95% CI, 1.27 to 4.51; P = 0.007; median 4.67 months versus 12.36 months).

Conclusion: Our study demonstrates that EUS-FNA shows high PPV in diagnosis of ASC, and our matched case-control study demonstrates ASC is more aggressive than PDAC.

P3 – 076
SEVERE ENCASEMENT OF SUPERIOR MESENTERIC ARTERY OR CELIAC ARTERY RELATES PAIN AND GASTROINTESTINAL SYMPTOMS IN PATIENTS RECEIVING CHEMOTHERAPY FOR ADVANCED PANCREATIC CANCER
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Background: Pancreatic cancer (PC) with severe arterial encasement (more than 180°) of the superior mesenteric artery (SMA) or celiac artery (CA) is considered unresectable. Severe arterial encasement is important for the management of PC patients, but its clinical significance in advanced PC is unclear. The aim of this study was to identify the impact of severe arterial encasement on symptoms, body composition, and outcome among patients receiving chemotherapy for advanced PC.

Methods: Patients with treatment-naive, unresectable PC and no obvious infectious conditions were eligible for enrollment. The symptoms were rated numerically from 0 to 10 using the Japanese version of the MD Anderson Symptom Inventory. Body composition was evaluated using a bioelectrical impedance analysis. The measurements were carried out before the start of chemotherapy. The overall survival time (OS) was calculated from the start of chemotherapy. Severe arterial encasement was defined as tumor abutment of the SMA or CA exceeding 180 degrees of the
circumference of the vessel wall on dynamic computed tomography images, as assessed by first author.

Results: Ninety-three patients (female/male: 44/49, PS 0-3: 66/26/1, median age: 66 years) were enrolled. All the patients received chemotherapy (GEM/GEM-based/S-1: 56/21/16). Severe arterial encasement and liver metastasis were found in 37 and 44 patients, respectively. Severe arterial encasement did not impact the OS (HR, 1.20; P = 0.427) but shortened the OS of patients without liver metastasis (HR, 1.99; P = 0.037). The severity of nausea and appetite loss and the dosage of morphine were higher in the severe arterial encasement group (P = 0.002, P = 0.025, P = 0.045, respectively). The fat mass tended to be lower among patients with severe arterial encasement (P = 0.037).

Conclusions: Severe arterial encasement is related to pain and digestive symptoms among patients with advanced PC and has a prognostic impact among patients without liver metastasis.

SYMPTOMATIC CHANGES TO PREDICT DISEASE CONTROL BY CHEMOTHERAPY FOR PANCREATIC CANCER

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Background: Alleviation of symptoms is related to good tumor control in patients undergoing systemic chemotherapy for pancreatic cancer (PC). The predictive value of symptomatic changes has not been fully understood. The aim of this study was to identify symptomatic changes that predict disease control by chemotherapy in PC patients (pts).

Methods: Pts with unresectable PC who had not received any anti-cancer therapy for PC were eligible for inclusion in this study. Pts with obvious infectious conditions were excluded. The symptoms and tumor markers of pts were prospectively assessed. Symptom severity was scored from 0 to 10 using the Japanese version of the MD Anderson Symptom Inventory before the start of chemotherapy and one month later. The tumor response was evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) ver. 1.0. Disease control was defined as CR, PR, or SD. An attempt was made to identify symptomatic changes that predicted disease control, and their impact on progression-free survival (PFS) was assessed.

Results: The number of pts was 87 (male/female: 46/41, Karnofsky performance status (KPS): 100/90/80/70-50: 32/29/17/9, median age: 66 years). Gemcitabine monotherapy (GEM), a GEM-based regimen, and S-1 monotherapy were carried out in 42, 41, and 4 patients, respectively. Disease control was observed in 31 patients. The rate of disease control was lower in pts with worsened sleep disturbance, distress, increased dose of morphine and CA19-9 than in pts without them (P = 0.004, P = 0.041, P = 0.015, P < 0.001, respectively). The multivariate analysis revealed that the worsened sleep disturbance (Odds ratio 3.94, P = 0.035) and increased CA19-9 (Odds ratio 3.63, P = 0.054) was predictive in poor disease control by chemotherapy. And the area under the ROC curve to diagnose disease control using worsened sleep disturbance (0.682) was similar with that using increased CA 19-9 (0.665).

Conclusions: The worsened sleep disturbance can predict poor disease control in PC pts undergoing chemotherapy.

Poster Session 60: Hepatobiliary cancer

SAFETY OF COMBINATION CHEMOTHERAPY WITH CISPLATIN AND GEMCITABINE FOR UNRESECTABLE BILIARY TRACT CANCER

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Background: Combination chemotherapy with cisplatin and gemcitabine (CG) has emerged as the standard treatment of advanced or recurrent biliary tract cancer (ARBTC) and has been introduced into the oncology practice in Japan since August 2011. The purpose of this study was to report the safety profile of CG regimen for ARBTC.

Methods: A total of 10 lesions were analyzed. All the lesions were from 3 cm (median 2 cm) were analyzed. The mean number of CRT cycles per patient was 2 (range 1-4). The median overall survival and progression-free survival were 13.2 months and 6.2 months, respectively. Severe arterial encasement did not impact the OS (HR, 1.20; P = 0.045) was the predictive marker in poor disease control by chemotherapy. We assessed the benefits of chemotherapy with GC after the failed GEM monotherapy before the ABC-02 era.

Method: We retrospectively examined the patients with advanced biliary tract cancer, treated with chemotherapy with GC after the failed GEM monotherapy. Eligible patients who had unresectable or recurrent biliary tract cancer, objective tumor progression after the GEM chemotherapy, adequate organ function including renal function and ECOG performance status (PS) 0-1. The treatment consisted of CDDP (25 mg/m² of body-surface area)-GEM (1000 mg/m²) on days 1 and 8, every 3 weeks.

Results: Between December 2010 and October 2011, 14 patients were enrolled to our study. Median age was 63 years. There were 11 males and 3 females. The ratio of intrahepatic bile ducts, extrahepatic bile duct, gall bladder was 6:4:4. The ratio of locally advanced and metastatic disease was 11:3. Severe arterial encasement did not impact the OS (HR, 1.20; P = 0.041, P = 0.015, P = 0.001, respectively). The results showed significantly lower V40 Gy, V30 Gy, V20 Gy, and V10 Gy than VMAT (1.54 ± 0.38 Gy) (P = 0.007). The mean dose (Dmean) for the organs at risk (OAR) and the maximal dose at 1% volume (D1%) for the spinal cord. The percentage of the liver volume receiving ≥240, ≥30 >20, and ≥10 Gy (V40 Gy, V30 Gy, V20 Gy, and V10 Gy) were also evaluated to determine liver toxicity.

Results: VMAT achieved significantly better CI values (1.02 ± 0.07) than VMAT (1.54 ± 0.38) (P < 0.001). The changes of VMAT, Dmean for the organs at risk (OAR) and the maximal dose at 1% volume (D1%) for the spinal cord. The percentage of the liver volume receiving ≥240, ≥30 >20, and ≥10 Gy (V40 Gy, V30 Gy, V20 Gy, and V10 Gy) were also evaluated to determine liver toxicity.

Conclusions: VMAT achieved significantly better CI values (1.02 ± 0.07) than VMAT (1.54 ± 0.38) (P < 0.001). The changes of VMAT, Dmean for the organs at risk (OAR) and the maximal dose at 1% volume (D1%) for the spinal cord. The percentage of the liver volume receiving ≥240, ≥30 >20, and ≥10 Gy (V40 Gy, V30 Gy, V20 Gy, and V10 Gy) were also evaluated to determine liver toxicity.

EVALUATION OF CHEMOTHERAPY WITH CISPLATIN-GEMCITABINE AFTER FAILURE OF GEMCITABINE MONOTHERAPY FOR UNRESECTABLE OR RECURRENT BILIARY TRACT CANCER

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Background: Because there was no standard chemotherapy for patients with advanced biliary tract cancer before the ABC-02 trial, we treated them with gemcitabine (GEM) alone. However, recently cisplatin (CDDP)-GEM (GC) became standard first-line chemotherapy. We assessed the benefits of chemotherapy with GC after the failed GEM monotherapy before the ABC-02 era.

Method: We retrospectively examined the patients with advanced biliary tract cancer, treated with chemotherapy with GC after the failed GEM monotherapy. Eligible patients who had unresectable or recurrent biliary tract cancer, objective tumor progression after the GEM chemotherapy, adequate organ function including renal function and ECOG performance status (PS) 0-1. The treatment consisted of CDDP (25 mg/m² of body-surface area)-GEM (1000 mg/m²) on days 1 and 8, every 3 weeks.

Results: Between December 2010 and 2011, 14 patients were enrolled to our study. Median age was 63 years. There were 11 males and 3 females. The ratio of intrahepatic bile ducts, extrahepatic bile duct, gall bladder was 6:4:4. The ratio of locally advanced and metastatic disease was 11:3. Severe arterial encasement did not impact the OS (HR, 1.20; P = 0.041, P = 0.015, P = 0.001, respectively). The results showed significantly lower V40 Gy, V30 Gy, V20 Gy, and V10 Gy than VMAT (1.54 ± 0.38 Gy) (P = 0.007). The mean dose (Dmean) for the organs at risk (OAR) and the maximal dose at 1% volume (D1%) for the spinal cord. The percentage of the liver volume receiving ≥240, ≥30 >20, and ≥10 Gy (V40 Gy, V30 Gy, V20 Gy, and V10 Gy) were also evaluated to determine liver toxicity.

Conclusions: GC can be an optional therapy for unresectable or recurrent biliary tract cancer after the failed GEM monotherapy.
Poster Session 61: Breast cancer chemotherapy

Efficacy and tolerability of gemcitabine for metastatic breast cancer

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Background: Metastatic breast cancer (MBC) still remain incurable and the goals of treatment are to prolong survival while controlling symptoms and minimizing toxicity. We evaluated the efficacy and tolerability of Gemcitabine (GEM) in MBC patients at our institute.

Methods: Clinical data from 17 MBC patients treated with GEM alone or with trastuzumab (in HER2 overexpressing patients) were retrospectively examined. Patient and tumor characteristics, best overall response, time to progression (TTP), adverse effects (CTCAE) were examined.

Results: Median age was 62 (40-81) and 5 (29%) received trastuzumab in combination with GEM. 15 were recurrent MBC after surgery and 9 (60%) had had adjuvant chemotherapy, with 7 receiving an anthracycline or a taxane. Median number of previous treatments was 3 regimens (range: 1 – 8 regimens). Best overall response was 1 CR (5.9%), 1 PR (5.9%), 4 SD (23.5%), 11 PD (64.7%) with a response rate of 11.7% and a clinical benefit rate of 17.6%. Median TTP was 3 months (range: 1–8 months). Adverse effects were three cases of grade 3 diarrhea, one case of fatigue, three cases of grade 3 neutropenia. Dose modification and delayed administrations were caused by neutropenia, diarrhea, and fatigue. Among the six responders, GEM was administered earlier (first or second line as MBC treatment) in four cases, but for the others, GEM was the sixth and seventh regimen.

Conclusion: GEM was well tolerated and could be a choice of treatment even in later regimens in MBC.

Poster Session 62: Breast cancer

A retrospective analysis of the breast cancer patients who survived long-term after recurrence

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Background: It seems to be difficult to conclude that patients with recurrent breast cancer can be cured. The prognoses of such patients, however, have been improved with the introduction of newer, more effective agents. We retrospectively reviewed the long-term survivors of recurrent breast cancer in order to clarify their clinicopathological characteristics.

Patients and methods: The clinical records of the breast cancer patients who survived more than 5 years after recurrence and treated between 1995 and 2011 at Iida Municipal Hospital were examined. Results: Thirteen patients have survived more than 5 years after recurrence. Mean age at operation was 46.5 years. Median disease-free interval was 90.8 months and median survival time after recurrence was 84.0 months. Hormone receptor and HER2 status of the primary site was ER+ and/or PgR+ and/or HER2- in 11, ER+ and/or PgR+ and/or HER2+ in 1 and ER- and/or PgR- and/or HER2+ in 2 patients respectively. All patients had nodal involvement. First site of relapse was bone in 4, lung in 4, liver in one, and locoregional site in 3 patients respectively. Mean number of metastatic sites was 1.9 (range 1–4) at 5 years after the occurrence of relapse. Patients have been treated with 5.5 (range 1–12) regimens since the relapse. ER+ patients were treated with 2.6 endocrine therapies and HER2+ patients were treated with regimens including trastuzumab. Radiotherapy was carried out for 2 patients with locoregional recurrence and one patient with bone metastasis.

Conclusions: The patients with ER+ and/or HER2+ breast cancer have survived longer than those with the other breast cancer after recurrence. Most long-term survivors have been sequentially treated with more than 2 different endocrine therapies or some combination regimens including trastuzumab, suggesting that the strategies with systemic therapeutic agents, such as aromatase inhibitors, trastuzumab, etc., would lead to prolonged survival for the patients with luminal A and/or HER2 subtypes of breast cancer.

Poster Session 63: Breast cancer/ Eribulin

Eribulin for the treatment of a patient with triple negative metastatic breast cancer - a case report-

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Background: Eribulin is an anti-cancer drug with a novel mode of action that inhibits microtubule dynamics. Triple-negative breast cancer is an aggressive type of breast cancer that is clinically defined as lacking estrogen and progesterone receptors, as well as being HER-2 negative, and carries a worse prognosis than other types of breast cancer. We report on an effective treatment with eribulin in a case with refractory triple-negative metastatic breast cancer.

Case: A 71-year-old woman had undergone total mastectomy and sentinel lymph node biopsy for stage II right breast cancer in August 2003. Immunohistochemical examinations of the tumor cells showed negative results for estrogen receptor, progesterone receptor and HER 2 (score: 0). After recurrence of multiple bone metastasis in November 2006, she received chemotherapy including FEC (epirubicin, cyclophosphamide and 5-fluorouracil) protocol, T5-1, or paclitaxel. Despite these treatments, clinical examination, serological data and CT findings revealed the evolution of the disease with bone and liver metastasis. She was referred to our department and was treated with eribulin as a novel therapeutic agent (1.1 – 1.2 mg/m², 2 weeks on, 1 week off). After 6 courses of administrations, a CT scan showed a marked improvement of liver metastasis. The level of cancer antigen 15-3 (CA 15-3), which was initially 922.8 U/ml (normal value of <31), lowered to 198.9 U/ml and the elevated CEA was normalized. No severe non-hematological adverse event above grade 3 was noted (peripheral neuropathy: grade 1, alopecia grade 1). Grade 3 neutropenia and leukopenia were observed in hematological adverse event, but febrile neutropenia was not experienced. She remains well and continues monotherapy of eribulin.
Case 1: A 77-year-old male saw a local doctor to complain stomachache. Therefore we experienced two autopsy cases of CUP that were treated as adrenal carcinoma. It is suggested that appropriate chemoradiotherapy for mediastinal lymph node carcinoma of an unknown primary site may offer a chance of long-term survival in patients who are not eligible for radical extention.

Case 2: A 68-year-old male saw a local doctor to complain fever and abdominal pain. Abdominal CT scan revealed an 8 cm tumor on the left of ventral aorta. We did biopsy of abdominal subcutaneous nodules and diagnosed poorly differentiated carcinoma. Therefore we experienced two autopsy cases of CUP that were treated as adrenal carcinoma. Case 1: A 77-year-old male saw a local doctor to complain stomachache. Abdominal CT scan revealed an 8 cm tumor on the left of ventral aorta. We did biopsy of abdominal subcutaneous nodules and diagnosed poorly differentiated carcinoma. Case 2: A 68-year-old male saw a local doctor to complain fever and abdominal pain. Abdominal CT scan revealed an 8 cm tumor on the left of ventral aorta. We did biopsy of abdominal subcutaneous nodules and diagnosed poorly differentiated carcinoma.

Conclusion: Second-line chemotherapy may be beneficent for unfavorable-risk CUP patients who had good response to first-line chemotherapy.

Poster Session 65: Palliative and supportive care clinical analize 3


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Objective: To evaluate the incidence and clinical characteristics of venous thromboembolism (VTE) in Japanese patients (pts) with solid malignancy at a single institution.

Patients and methods: Pts with solid malignancy who were treated in our department from July 2007 to December 2011 were retrospectively reviewed from medical records.

Results: 750 pts with solid malignancy were analyzed. A total of 18 cases (2.4%) were complicated with VTE. Median age at the diagnosis of VTE was 63 years (range: 31–76), and 12 pts were women and 6 pts were men. Eleven cases were complicated with deep vein thrombosis (DVT) and 7 with both pulmonary embolism (PE) and DVT. Symptoms at the initial diagnosis of VTE were swelling of extremities (15/18: 83%), pain in extremities (3/18: 17%), dyspnea (1/18: 7%), and incidental detection of VTE on follow-up imaging study without symptoms (3/18: 17%). Diagnostic procedures of VTE were contrast-enhanced CT in 11 pts (67%) and venous ultrasonography in 16 (89%). The location of the involved veins was the upper limb in 5 pts, lower limb in 12, and inferior vena cava (IVC) in 1. PE was bilateral in six of seven pts. Primary sites of cancer included colorectum (six), pancreas (five), breast (three), lung (one), mediastinum (one), ovary (one) and stomach (one). A total of 13 pts (72%) had metastatic disease. Fifteen pts (83%) had been diagnosed with VTE during chemotherapy, with a median time from the initiation of chemotherapy to diagnosis of VTE of 169 days (range: 3–1363). Central venous port (C-V port) systems were inserted in 6 of 18 pts (33%). Among the 5 pts with DVT in the upper limb, 4 received C-V port insertion. Regarding treatment of VTE, 17 of 18 pts received anti-coagulation therapy with heparin and/or warfarin and 3 of 18 received IVC filter placement.

Conclusion: The incidence and clinical characteristics of cancer-related VTE at our institution are closely similar to those previously reported from western countries. Consideration of cancer-related VTE is also required in Japanese populations.
Results: Retention times of these drugs were Ara-C (m/z 244.0/112.0) 1.20 min, GEM (m/z 264.0/112.0) 2.20 min, MTX (m/z 455.1/308.2) 6.21 min, ETP (m/z 691.0/ 691.0) 9.51 min, IFO (m/z 261.1/92.2) 11.5 min, CPA (m/z 261.1/92.2) 12.3 min, CPT; 11 (m/z 587.3/167.2) 7.34 min, ADR (m/z 544.1/310.1) 7.64 min and EPI (m/z 544.1/310.1) 8.15 min, respectively. The same molecular weight compounds (m/z: 554.1 ADR and EPI m/z 261.1 IFO and CPA) were separated by the reverse-phase LC gradient.

Conclusions: We established the method to detect multicytotoxic drugs from wipe samples on occupational environment. In the future, we will investigate for environmental exposure to cytotoxic drugs in the various hospitals.

Poster Session 66: Palliative and supportive care clinical analyze 4

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Background: The increasing use of complementary and alternative medicine in Western countries and Asian population was reported in recent 10 years. The purpose of this study is to investigate patterns of the use of traditional Chinese medicine (TCM) in cancer patients in Taiwan.

Methods: We used insurance claims data from the National Health Insurance Research Database, a universal insurance program with a coverage rate of more than 99% of the population in Taiwan. We identified 21,401 patients with newly diagnosed cancer during the period 1997–2008. The records of TCM use after cancer diagnosis within 1 year were collected. This study calculated odds ratios (ORs) and 95% confidence intervals (CIs) of factors associated first-year TCM use in cancer patients by using multivariate logistic regression analysis.

Results: The first-year prevalence of TCM use in cancer patients was 29.2%. The first-year TCM use for cancer patients in 1997 was 24.8% increased to 32.6% in 2008. Women (OR = 1.15, 95% CI = 1.07–1.23), higher income (OR = 1.26, 95% CI = 1.13–1.40) and previous TCM use experience (OR = 4.40, 95% CI = 4.12–4.69) were factors associated with first-year TCM use in cancer patients. In subtypes of cancer patients, the highest average of TCM visits and medical expenditure in men and women were breast cancer patients (6.6 ± 7.8 visits, 120 ± 141 USD) and bladder cancer patients (8.2 ± 12.4 visits, 153 ± 231 NTD), respectively.

Conclusions: TCM use is common among cancer patients in Taiwan. The interactions between TCM herbal medicine and western medicine pharmaceuticals need concerns.

Poster Session 09: Palliative and supportive care/bone metastasis

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Preoperative chemoradiotherapy for rectal cancer aims to decrease the local recurrence after the surgery. This measure adopted as a standard treatment internationally, however various symptoms caused by tumor could obstruct the preoperative treatment because 10-12 weeks are required before surgery. Among them, tumor pain caused by the invasion into surrounding tissue could be a big and prolonged problem during the treatment. In four cases of lower rectal cancer complicating of severe anal pain on first admission, we planned preoperative chemoradiotherapy with supporting treatment including administration of NSAIDs with or without opioids. After 4 weeks of chemoradiotherapy, all the patients could reduce of the amounts of the drugs. After preoperative chemotherapy as planned, all of them had curative surgery consecutively. The preoperative chemoradiotherapy for oncological safety must be carried out with special interest, care and treatment on the anal pain caused by rectal cancer.

Poster Session 70: Leukemia/MDS/CML/HS

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Gemtuzumab ozogamicin (GO), an anti-CD33 monoclonal antibody conjugated calichamicin, has approved as a single agent in Japan for relapsed/refractory acute myeloid leukemia (AML). Complete remission rate was reported only as 30% in a...
CRONIC MYELOGENOUS LEUKAEMIA FOLLOWING S-1 THERAPY FOR RECTAL CANCER: A CASE REPORT

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Introduction: Therapy-related leukemias are one of the most common second malignancies. However therapy-related chronic myelogenous leukemia (CML) is far more rare than therapy-related acute myeloid leukemias or myelodysplastic syndromes. Here we report a case of secondary CML, who had a past history treated with S-1 as post-operative therapy for rectal cancer.

Case report: A 59-year-old male was referred to our hospital because of leukocytosis on October 2011. His laboratory findings showed a white blood cells of 14 × 10^9/l with 11% basophils, 7% eosinophils, 0.5% lymphocytes, 66.5% neutrophils. His haemoglobin level was 11.9 g/dl and his platelet count was 393 000/ul, and his serum level of lactate dehydrogenase was 341 U/I. He had a past history of rectal cancer received abdominoperineal resection in July 2008, and was subsequently treated with oral anti-metabolite S-1 for a year (total dosage of 33 600 mg). Bone marrow aspirate showed hypercellular bone marrow without blast increase, and karyotype analysis revealed 46.XY(9;22)(q34.1;11.2) [20]. A diagnosis of therapy-related CML was made because of his past history of S-1 therapy. The patient was started on dasatinib therapy and rapidly achieved complete haematological remission.

Discussion: S-1 is among the most effective anti-cancer agents for various carcinomas such as gastric cancer, lung cancer and biliary tract neoplasms. And for colorectal cancer, S-1 is recommended as a suitable treatment of adjuvant therapies. To best of our knowledge, only few cases of therapy-related CML following fluoropyrimidines therapy have been described. The frequency, clinical course and prognostic value of therapy-related CML has not been clarified yet because of its rarity, and further accumulation of cases is necessary for evaluation of the therapeutic outcome of therapy-related CML patients.

HISTIOCYTIC/DENDRITIC NEOPLASM WITH MARKED BLOOD COAGULATION DISORDER

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Tumors of histocytes are among the rarest of tumor affecting lymphoid tissues. As these tumor types were poorly recognized until recently, it is sometimes difficult to establish diagnosis and their clinicopathological features are still obscure. Here, we report a case of histiocytic/dendritic neoplasm with marked blood coagulation disorder. A 71-year-old woman was admitted to the hospital for progressive abdominal distention and bilateral cervical lymphadenopathy lasting for a month. Computed tomography scan showed marked hepatosplenomegaly and ascites and low gastrointestinal endoscopy showed ileal neoplasm. Pathological findings of the tumor showed proliferation of large pleomorphic cells with abundant and eosinophilic cytoplasm and infiltration with small T-lymphocytes. She was suspected with malignant lymphoma and transferred to our hospital after one week from her first hospitalization. On admission, her performance status was 3 and she showed systemic subcutaneous bleeding and marked abdominal distention. Her laboratory data showed marked blood coagulation disorder (PT 2.6 × 10^3/s, INR 1.74, APTT 51.1 s, Fb 60 mg/dl, AT III 14%, FDP 2.8 µg/ml, PIC -0.3, TAT 31.4 µg/ml) and liver dysfunction (T-Bil 3.1 mg/dl, LDH 528 U/L, AST 98 U/L, ALT 685 U/L, ALP 685 U/L). We had to abandon lymph node biopsy for definitive pathological diagnosis because of her severe coagulopathy but bone marrow aspirate examination revealed 14% of large abnormal cells resembling ileal tumor cells which were positive only with CD3, CD13, CD10, HLA-DR and negative with other lymphoid markers. B- and T-cell histiocytic lineage markers excepting CD5 of t-cell tumor were also absent but S-100 protein was positive. Her disease was distinguished from malignant lymphoma and diagnosed as histiocytic/dendritic neoplasm. She wanted to keep palliative care and passed away at three weeks after her first hospitalization.

SCREENING FOR HEPATITIS B VIRUS CARRIERS AND THE INCIDENCE OF HEPATITIS B REACTIVATION IN PATIENTS WITH MALIGNANT LYMPHOMA AT OUR INSTITUTION

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Background: Hepatitis B virus (HBV) reactivation is a rare but serious complication in cancer patients undergoing chemotherapy, especially those receiving rituximab and steroids. In this prospective study, we screened lymphoma patients for the HBV infection status before the start of chemotherapy, and evaluated the incidence of HBV reactivation after chemotherapy: furthermore, we also evaluated the efficacy of entecavir treatment.

Methods: Malignant lymphoma patients aged 16 years or over, newly diagnosed at our institution between January 2010 and December 2011, were enrolled. Serologic tests for HBs antigen (HBsAg), HBs antibody (HBsAb), HBe antibody (HBeAb) were carried out in all patients before the start of chemotherapy. In the patients with positive test results, chemotherapy was administered as usual. In the patients, positive for any serum marker of HBV infection, HBV-DNA testing was carried out. If positive, entecavir was started. If negative, HBV-DNA was measured once a month, and if/when the results turned positive, entecavir was started and the chemotherapy continued.

Results: Among the 103 patients, 50 patients were positive for HBsAg, 30, for HBsAb, or HBeAb. Among the patients who were HBsAg(+), HBsDNA(+), and HBeAb+ and/or HBsAb+ (47 patients), two patients (4%) became positive for HBV-DNA and needed entecavir treatment. In three patients who were HBsAg+ prior to the chemotherapy, chemotherapy was started after administration of entecavir. Among the patients who needed entecavir (five patients), none developed fulminant hepatitis, and HBV-DNA test became negative within 2 months of entecavir administration.

Conclusions: The incidence of HBV+ patients at our institution was high as compared with that in previous reports from other area in Japan. The rate of and risk factors (male, HBsAb negative) for HBV reactivation were comparable with those reported previously. In patients who become HBV-DNA positive, entecavir administration effectively prevented fulminant hepatitis.

INVESTIGATIN OF A DISSEMINATED VARICELLA IN LYMPHOMAPATIENT TREATED WITH RITUXIMAB COMBINED CHEMOTHERAPY

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Background: Rituximab containing regimen has improved the outcome of B-cell lymphoma. One of the problems of rituximab-related infection is latent virus reactivation, for example, hepatitis B virus and JC virus. However, the possibility of increasing the susceptibility to varicella is unknown. In several rituximab containing trials, an increase in the community-acquired infection has not been reported. Here, we report a cluster case of varicella patients treated with rituximab containing chemotherapy.

Case report: We diagnosed four cases from 18 May 2011 to 19 June 2011. All patients were diffuse large B cell lymphoma patients treated with rituximab containing regimen. These patients were hospitalized in two hematological wards and each patient stayed different room. When we diagnosed varicella, we moved the patient to negative pressured room and started universal precautions. All patients were treated with acyclovir. Three mild patients had treated for 7 days. Another severe patient had treated for 5 weeks. We examined anti-VZV antibody in prechemotherapy serum and all those represented post-infection pattern. We analyzed VZV DNA sequence in gene 62 which has diverseness, and all sequences were treated with acyclovir. Three mild patients had treated for 7 days. Another severe patient had treated for 5 weeks. We examined anti-VZV antibody in prechemotherapy serum and all those represented post-infection pattern. We analyzed VZV DNA sequence in gene 62 which has diverseness, and all sequences were the same. Therefore, we deduced that they were infected with identical VZV.

Conclusion: Rituximab has possibility of increasing the reinfection of varicella.
Reports on the efficacy of intravenous immunoglobulin (IVIG) prophylaxis against cytomegalovirus (CMV) infection after allogeneic hematopoietic cell transplantation (HCT) have often sparked controversy. In addition, we are not aware of any study that has examined whether prophylaxis with IVIG affects the incidence of CMV infection in patients who are at high risk of infection; those who are elderly or have received HLA-mismatched HCT. In our report, high incidence of heart failure in patients who received HD-AC, and cardiac function should be carefully monitored in such cases.

**Conclusions:** In our hospital, 10 patients received HD-AC as first consolidation therapy. In 4 heart failure patients, 3 were suffered from sepsis. On the other hand, 10 patients received conventional consolidation therapy. 3 patients suffered from sepsis (eight events), but there were no findings of heart failure. Therefore, we consider that in the patients received HD-AC therapy, heart failure appears severely initiated by infection. Several pericarditis or arrhythmia caused by HD-AC had already reported, although almost all reports were single case report. In conclusion, our report highlighted a high incidence of heart failure in patients who received HD-AC, and cardiac function should be carefully monitored in such cases.

**Methods:** We collected medical information from patients who received HD-AC at our hospital from April 2002 to August 2010. We also compared with patients who received conventional consolidation therapy between July 1998 and July 2011.

**Results:** Their mean age is 45.8 (28–58), 3 of them are female. Three patients are CBF leukemia (two are (8:21), one is inv(16). All of them achieved complete remission by remission induction therapy. They received HD-AC as consolidation therapy. Mean of ejection fraction was decreased from 67.7 to 47.3%. 3 patients were recovered with in 2 week. Only one patient, it was required for 6 months to recover.

**Discussion:** Although the number of patients in this series is small, it appears that survival rate with a median follow-up of 6.3 years is 62.5% (10/16). The clinical aspects and problems in adolescents and young adults (AYA) with cancer in the western countries have been elucidated. These patients have benefited less from therapeutic advances partly because of less opportunity to participate in clinical trials. And AYA cancer patients have many social problems such as school, employment and expense. This situation is called as AYA gap and some programs have been started in the USA to improve the outcome of AYA cancer patients as an orphaned population. AYA cancer patients have not been studied in Japan and we do not have any available nation-wide data of this population. Here, we report AYA cancer patients who were treated at Osaka Medical Center and Research Institute for Maternal and Child Health (OMCRI). Sixteen AYA cancer patients aging from 15 to 29 years were treated at OMCRI during 2005–2009. These cases were analyzed in terms of diagnosis, age, treatment, and outcomes.

**Discussion:** Although the number of patients in this series is small, it appears that incidence and characteristics of AYA cancer patients in Osaka is similar to that of USA. These results suggest the importance of a multimodal combination therapy for the treatment of AYA cancer patients. Approximately 250 young people aged 15–29 are annually diagnosed with cancer in Osaka prefecture, and cancer is the leading cause of death in this age population. Therefore, it is important to analyze the incidence, situation of medical-examination, treatment and outcome of AYA cancer patients in the large scale. We recently organized an AYA cancer information-sharing system (Osaka AYA Cancer Network) including specialists such as pediatric or adult hematono-cologist, epidemiologist, and so on to understand and investigate AYA cancer patients in Osaka area in an attempt to improve the outcomes and quality of life for these patients.