assess whether surgical intent (curative or cytoreductive) has an impact on long-term outcome, and assess cost-effectiveness of surgery for the symptomatic management of hepatic neuroendocrine metastases.
Methods: A retrospective review of a prospectively maintained database of all patients referred to a neuroendocrine multidisciplinary team meeting between January 1996 and December 2008.
Result: 340 patients were referred during the study period, of whom 190 (55.8%) had disease stage 1−3. Of the remaining 150 patients with stage 4 disease, 117 (78%) were treated non-surgically (6 RFA, 15 MIBG, 51 octreotide, 23 lantreotide, 2 dotate, 2 chemoembolisation) whilst 33 patients (22%) were treated by surgical resection. Thirteen underwent surgery with curative intent, whilst 19 underwent cytoreductive resection. At median follow-up of 66 months, 8 of the 13 patients (62%) who underwent curative resection had hepatic recurrence. Overall 1, 3, and 5-year survival rates were 94%, 64% and 46% for stage 4 medically medically managed patients, 100%, 100% and 82% for patients undergoing cytoreductive surgery and 100%, 100%, 100% for patients undergoing curative resection. (p = 0.049). Curative resection gave a median duration of symptom control of 67.5 months (IQR 36.5−81) compared to 24 months (IQR 19–45.5) for cytoreductive surgery. Cost per QALY for the treatment of hepatic neuroendocrine metastases was €1,438 for curative surgery and €3,121 for cytoreductive surgery, compared to €14,450 for non-surgical management.
Conclusions: Hepatic resection improves survival in patients with neuroendocrine metastases. Although recurrence rates are high, curative surgery is associated with more durable symptom control than cytoreduction. Resection for symptom control is considerably more cost-effective than medical management.

6517 POSTER

Sunitinib and Transarterial Chemoembolization (TACE) for Advanced Hepatocellular Carcinoma (HCC)- Final Results of a Phase 2 Trial

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Background: TACE and oral anti-angiogenic agents have individually been effective for treating inoperable HCC. We evaluated the effects of a combination of sunitinib and TACE on PFS in this prospective phase 2 study.
Methods: Eligibility: PS 0, 1, inoperable HCC, Child Pugh A or B, platelets >100K, bilirubin 2 or less and no contraindication to TACE. Treatment: Cycle (C)1-Sunitinib 37.5 mg po day (d)1−7 followed by TACE with doxorubicin in lipodiol on d8, continued sunitinib 37.5 mg po qd d15−36 followed by 2 weeks off. C2 onwards- sunitinib 4 weeks on and 2 weeks off, with dose escalation to 50 mg in patients (pts) without any grade 3 toxicities in C1. DCE MRI, sVEGFr, monocytes, and sunitinib PK were assessed at baseline, d 8, 10 and 36.
Results: Baseline characteristics of 16 pts were following: median age 74 years (range 40−86), 12 males and 4 females, all with Child Pugh Class A cirrhosis (etiology: hepB: 2, hepC: 6, alcoholic: 1, unknown: 7), and ECOG PS 0: 12 and PS 1: 4. There were 10 liver only and 6 extrahepatic disease sites. Median PFS was 8 mo (95% CI 4.3−9.3) and OS was 14.9 mo (95% CI 6.3–27.1) with a median follow up of 12.8 months, and 5 patients still alive. Responses by RECIST criteria were 2 PR,11 SD, and 3 clinical deteriorations; clinical benefit rate was 81%. Median number of cycles on study was 3 (range 1−7). For 8 pts with DCE- MRIs, median Ktrans change was −20% after 7 days of sunitinib and a 7% further decrease was seen after TACE and sunitinib; decrease in viable tumour at same timepoints was 3% (d8) and 15% (d36) respectively. Steady-state sunitinib concentrations ranged from 20–150 ng/mL, which were above the IC_{50} values of 4−30 ng/mL for VEGF inhibition. PK/PD modeling estimated sunitinib IC_{50} values of 15 and 10 ng/mL for modulation of Ktrans and AUC_{90}. sVEGFR2 levels increased with Ktrans and AUC_{90}. Median monocyte counts were 0.4 x 10 x9/L before and decreased by 50% on d36 after TACE. Eleven pts (69%) had grade 3/4 toxicities attributable to sunitinib. Of the 57 total events, the most frequent (n = 5 or more) were thrombocytopenia (10), amylase/lipase increase (9), lymphopenia (7) and fatigue (6). Dose delays and dose reductions occurred in 13 and 3 patients respectively. Reasons for discontinuing therapy were toxicity (7), progression of disease (7) and withdrawal of consent (2).
Conclusions: This is the first study of sunitinib and TACE in HCC. Improvement in PFS and OS was seen with acceptable toxicity. Our studies show a relationship between sunitinib concentration and following markers: Ktrans, AUC_{90}, $sVEGFR_2$ and monocytes, with additional decrease seen after TACE.

6518 POSTER

Neoadjuvant Chemoradiotherapy for Locally Advanced Esophageal Cancer − Analysis of Pattern of Recurrence and Prognostic Factors for Survival

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Background: Concurrent chemoradiotherapy (CRT) followed by esophagectomy has become a standard treatment option in patients with resectable esophageal cancer. We analyzed pattern of recurrence and factors predictive for survival to find additional strategies to improve outcome.
Material and Methods: Between 2003 and 2009, 64 patients were treated with neoadjuvant chemoradiation followed by surgery as a planned approach for locally advanced esophageal cancer in our institute. All demonstrated a clinical T-stage of 2 or higher and histology was squamous cell carcinoma in all patients. The average age was 62.1 years, and most patients were male (89%). 14 patients (22%) had cStage II, 41 (64%) had cStage III and 9 (14%) had cStage IVa carcinomas (UICC-TNM 6th). A total of 36 patients received a combination of docetaxel and 5-Fluorouracil (5-FU) while 27 patients received a combination of cisplatin and 5-FU, and one received a combination of nedaplatin and 5-FU. The radiation was administered concomitantly and total dose was 40 Gy. Surgical resection was performed 4−6 weeks after the completion of chemoradiotherapy, using a right transthoracic approach with two- or three-field lymph node dissections.
Results: The overall clinical response rate to neoadjuvant CRT was 93.8%; 9 showed complete response (CR), 51 showed partial response (PR). On examination of the resected specimens, pathological CR was achieved in 16 patients (25%). Another 22 patients (34%) had a significant tumour response with only minimal tumour remaining. According to the clinical stage before CRT, 5-year survival was 75% in cStage II, 45% in cStage III and 27% in cStage IVa. Among 44 patients who were followed-up beyond 2 years, 22 patients experienced disease progression. Of the treatment failures, 8 (18% of 44 patients) were distant, 8 (18%) were locoregional, and 6 (14%) were both locoregional and distant failure. In patients who achieved pathological response, 2 courses of additional chemotherapy after surgery prolonged survival compared to patients without postoperative chemotherapy (p < 0.001), while no difference was seen in patients who had no pathological response. By multivariate analysis clinical response to neoadjuvant CRT (HR 0.09; p = 0.0003) and pathologic response (HR 4.17; p = 0.001) were factors predictive of overall survival.
Conclusions: As compared with our previous data of treatment failures in patients who underwent surgery alone, locoregional recurrence rate decreased, while distant recurrence rate did not change. Control of distant recurrence is considered to be the most important problem. In multivariate analysis, clinical and pathological response to neoadjuvant CRT were significant predictor of survival. Therefore, new CRT protocol that affects both locally and systemically including multi-agent chemotherapy or molecular targeting drugs should be needed to improve survival.

6519 POSTER

Role of Surgical Resection in Complete Responders on FDG-PET After Chemoradiotherapy for the Locally Advanced Esophageal Cancer

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Background: Trimodality therapy has been a standard treatment for locally advanced esophageal cancer, and definitive chemoradiotherapy (CRT) is an alternative treatment for unresectable or medically inoperable cases. But in patients who have a good response to CRT, the role of surgical resection is not clearly verified. The purpose of this study is to determine the prognostic significance of metabolic response and what the role of surgery is in complete responders on [^{18}F]Fluorodeoxyglucose positron emission tomography (FDG-PET) after CRT for locally advanced esophageal cancer.
Material and Methods: We retrospectively reviewed 162 patients with locally advanced esophageal cancer with increased uptake on FDG-PET before chemoradiotherapy. Of these, 89 patients received definitive CRT and 73 patients received surgery after preoperative CRT. FDG-PET was repeated 1 month after CRT, and metabolic complete remission (PET-CR) was defined as standard uptake value (SUV) of 3 or less. Overall survival (OS), disease free survival (DFS) and local recurrence free survival (LRFS) rates were compared between the two groups.

Results: Median follow-up time was 23.8 months (range, 3.5–76.5 months). Of 162 patients, 42 of 89 (47.2%) definitive CRT and 42 of 73 (57.5%) preoperative CRT patients achieved PET-CR. The 2-year OS of trimodality and definitive CRT groups were 61.6% and 39.3%, respectively ($p = 0.0106$). But it was 57.1% in PET-CR subgroup among definitive CRT patients and which was equivalent to that of trimodality group ($p = 0.736$). The 2-year LRFS was higher in trimodality group than in entire definitive CRT or PET-CR subgroup among definitive CRT patients (88.1% vs 56.8% and 62.3%, respectively, $p = 0.002$). The 2-year DFS was also higher in trimodality than in both entire CRT and PET-CR subgroup (72.8, 38.2% and 47.3%, respectively, $p = 0.007$). On multivariate analysis on prognostic factors, PET-CR was the only factor which was significant for OS (hazard ratio (HR) 2.076, $p < 0.001$), LRFS (HR 2.295, $p = 0.001$), and DFS (HR 2.050, $p < 0.028$). Surgical resection was also significant for LRFS (HR 2.674, $p < 0.001$) and DFS (HR 4.501, $p < 0.001$), but marginally significant for OS (HR 1.530, $p = 0.053$).
Conclusions: Trimodality treatment showed superior outcomes than definitive CRT in OS, DFS, and LRFS. When trimodality was compared to PET-CR subgroup of CRT patients, it was also beneficial in DFS and LRFS. It seems that surgical resection should be reserved as a component of current standard treatment until prospective study verify a subgroup which can omit surgical resection.

6520 POSTER

Concurrent Chemoradiation as Definitive Treatment in Anal Squamous Cell Carcinoma − Efficacy and Safety in HIV+ Patients Under HAART

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Background: HIV seropositivity is a known risk factor for anal squamous cell carcinoma (ASCC), but the efficacy and safety of concurrent chemoradiation (CRT) as definitive therapy for ASCC in HIV+ pts under highly active antiretroviral therapy (HAART), in comparison with HIV-negative/unknown ASCC pts, remains under discussion.
Materials and Methods: We retrospectively analysed all consecutive pts diagnosed and treated in a single institution from Apr/2000 to Jun/2010. Definitive CRT consisted of 45−54 Gy (180 cGy/d, 5 fractions/week), with concurrent mitomycin-C 15 mg/m^2 D1 IV and 5-fluoruracil (5FU) 1 g/m^2/d IV, continuous infusion, D1-D4 and D29-D32. The same treatment was delivered irrespective of HIV-status. HIV+ pts were under HAART according to standard recommendations.
Results: 102 pts were studied: median age 57 y (23−86 y), 83% female. Stage: Tis (3 pts), I (5), II (36), IIIA (15), IIIB (30), IV (4). Eleven pts were identified as HIV+. They were younger (41.2 vs. 60.1 y, $p < 0.0001$) and predominantly male (10/11). Mean CD4 count was 412±160 cells/microliter (210–664). No difference in tumour stage was detected. For all pts, the median dose of RT was 45 Gy, delivered over 46 d. No difference in terms of treatment duration or administered CRT intensity between HIV+ or HIV-negative/unknown pts was observed. Treatment was well tolerated and only one treatment-related death was seen in a pt with unknown HIV-status. 84 pts were evaluated for response, and complete response (CR) was achieved in 59 pts (70%). No difference was seen in HIV+ pts [7/9 CR (77.8%), $p = 0.890$] in terms of CR rate. With a mean follow-up of 23 months, 17 deaths have occurred. Overall, the median overall survival (mOS) was not reached (NR) and the 2-year OS rate was 79%. No difference in mOS was seen between HIV+ or HIV-negative/unknown pts (NR in both groups, HR 2.03, 95% CI 0.38–7.73, $p = 0.480$), and a 2-year OS rate of 89% was observed in HIV+ pts. Longer 2-y OS rate was observed in those pts that needed no colostomy (85% vs. 63%, HR 0.33, 95% CI 0.05–0.89, $p = 0.034$), and also in those pts who achieved CR after concurrent CRT (97% vs. 21%, HR 0.06, 95% CI 0.00–0.04, $p < 0.0001$).
Conclusions: In this group of ASCC, no differences in terms of efficacy and safety of concurrent CRT as definitive therapy for ASCC were detected based on HIV seropositivity. 5FU/MMC-based CRT can be delivered successfully in HIV+ pts under HAART.

6521 POSTER

Prospective Randomized Controlled Phase II Trial of Alternate-day Vs Consecutive-day Treatment With S-1 as Postoperative Adjuvant Therapy for Gastric Cancer: San-in Clinical Oncology Group Study No. 9

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Background: The adverse effects of S-1 can lead to discontinuation of treatment. In the ACTS-GC study, 28% of patients discontinued S-1 because of adverse events and 42.4% of the patients required dose reduction. Strategies for reducing toxicity without compromising therapeutic efficacy are required.
Methods: We prospectively examined 70 eligible patients with stage II or III gastric cancer who received S-1 on alternate-days (AD) or on consecutive-days (CD) following curative gastrectomy between November 2005 and October 2008. S-1 (80 mg/m^2 per day) was orally administered twice daily for 4 weeks, followed by a 2-week rest during 1 year in the CD group (standard regimen established by ACTS-GC) and was administered every other day for 1.3 years in the AD group. The planed administration schedule was 224 days in both groups. The primary end points were treatment accomplishment rate and relative dose intensity.
Results: We randomly assigned 35 patients to the AD group and 35 to the CD group. The two groups were well balanced with regard to clinical characteristics, surgical procedures and pathological findings. The complete clinical data was obtained from 31 patients in each group. The treatment accomplish rate was 93.5% (n = 29) in the AD group and 74.2% (n = 23) in the CD group. The relative dose intensity was 85.6% in the AD group and 72.1% in the CD group. The rates of grade 1−3 adverse events in the AD and CD groups were respectively as follows; 46% and 19% in anorexia, 29% and 14% in diarrhea, 20% and 5% in nausea, and 20% and 14% in mucositis. With a median follow-up duration of 18 months, the 1-year overall survival rates were 96.9% in the AD group and 93.8% in the CD group.
Conclusions: The AD group revealed a higher treatment accomplish rate and higher relative dose intensity than the CD group. Therefore, alternate-day treatment with S-1 may have milder adverse effects without compromising therapeutic efficacy.

6522 POSTER

Neoadjuvant Chemoradiation Therapy With Gemcitabine for Cholangiocarcinoma − Three-years Results After Phase I Study and Interim Analysis of Phase II Study

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Background: To improve the prognosis of cholangiocarcinoma, we are applying neoadjuvant chemoradiation therapy for cholangiocarcinoma (NACRAC) followed by conventional resection for possibly resectable cholangiocarcinoma. Three years have passed since Phase I study (P-1), and Phase II study (P-2) has been continued. Here, we evaluated the three-years' safety of P-1 and the feasibility of P-2.
Material and Methods: P-1 was designed to determine the recommended dose (RD) of gemcitabine. Patients with histologically or cytologically confirmed adenocarcinoma of the extra and hilar cholangiocarcinoma were enrolled from August 2007 to June 2008 at Tohoku University Hospital. The RD of gemcitabine was determined as 600 mg/m^2 with external beam radiation therapy (1.8-Gy daily fractions to a total dose of 45 Gy). NACRAC did not increased peri-operative complications like operative duration, surgical site infection (SSI), and hospital stay. Original results of P-1 were presented at European Society of Surgical Oncology 2008 (ESSO). P-2 was started in March 2009 at Tohoku University Hospital. Quality control of radiation therapy is very difficult, and then P-2 was started at our hospital only. The aim of this interim analysis is to evaluate pathological curability and adverse events. And assess the feasibility of this trial. The primary endpoint is rate of no residual tumour (R0-resection rate).
Results: Twelve patients were enrolled in P-1. After three years, seven patients were died because of primary disease. The most remarkable point is there is no severe adverse event and vascular occlusions related with radiation therapy while three years. This showed NACRAC with conventional resections were safe and tolerable. In P-2, 14 patients have enrolled. 8 patients were male, and 6 patients were female. Median age was 70.5 years old. 2 patients were not able to operated; one was not enough liver function for operation, and the other was occurred heart