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

failure. 12 patients were operated. Operative procedures were Pancreatico-duodenectomy, extended hemi-hepatectomy with bile duct resection, and bile duct resection were 6 cases, 4 cases, and 1 case, respectively. One patient was not resected by dissemination, which was found after laparotomy. 7 patients were operated with R0-resection, 4 patients were R2-resection. The factors of R2 were mainly distant metastases, this means NACRAC provided good local control. Based on Intention to treat (ITT) analysis, R0-resection rate was 57.1% (8 /14). This has possibilities to meet the primary end point, and then we continue P-2.
Conclusions: Three-years results after Phase I showed no severe adverse events, and P-2 showed acceptable effect as previously estimated. Neoadjuvant chemoradiation therapy with conventional resections appears to be effective and well tolerated. The study is continued as scheduled, to further evaluate the benefit of this regimen.
Trial registration: UMIN Clinical Trials Registry (UMIN-CTR) UMIN UMIN000000992 and UMIN000001754

6523 POSTER

Intraperitoneal Paclitaxel Combined With S-1 Plus Intravenous Paclitaxel for Gastric Cancer With Peritoneal Metastasis − a Report of 100 Cases

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Background: Peritoneal metastasis is the most life-threatening metastasis in patients with gastric cancer, and no standard therapy has been established in spite of recent advances in chemotherapy. We previously verified the safety and efficacy of S-1 plus intravenous (IV) and intraperitoneal (IP) paclitaxel (PTX) in phase I and II studies (Oncology 2009, Ann Oncol 2010). We hereby report the results of 100 patients treated with this regimen at the University of Tokyo Hospital.
Materials and Methods: Gastric cancer patients with macroscopic peritoneal metastasis were implanted with peritoneal access ports, and received combination chemotherapy of S-1 plus IV and IP PTX. PTX was administered IV at 50 mg/m^2 and IP at 20 mg/ m^2 on days 1 and 8. S-1 was administered at 80 mg/ m^2/day for 14 consecutive days, followed by 7 days rest. Radical gastrectomy was performed when macroscopic curative resection was made achievable after the chemotherapy. Efficacy and safety were evaluated in all the patients.
Results: Between February 2005 and January 2011, 100 patients with peritoneal metastasis were treated, including 80 with primary tumours, 10 after palliative gastrectomy, and 10 with peritoneal recurrence. The median number of courses was 8 (range 1−48). The median survival time (MST) was 22.6 months (95% CI, 17.9–28.9 months). The MSTs of subgroups were as follows: Metastasis to the adjacent peritoneum, 49.6 months (n = 10); metastases to the distant peritoneum, 19.7 months (n = 90). Ascites negative, 39.3 months (n = 29); ascites positive, 19.0 months (n = 71). With primary tumours, 20.6 months (n = 80); after palliative gastrectomy, 49.6 months (n = 10); with peritoneal recurrence, 22.6 months (n = 10). Out of 80 patients with primary tumours, 37 patients underwent gastrectomy after response to chemotherapy, and had a MST of 34.9 months. The frequent grade 3/4 toxic effects included neutropenia (36%), leukopenia (20%) and anemia (8%). Infection and obstruction of peritoneal access device were observed in 7 and 6 patients, respectively. There were no treatment-related deaths.
Conclusions: Combination chemotherapy of S-1 plus IV and IP PTX is well tolerated and active in gastric cancer patients with peritoneal metastasis.

6524 POSTER

Does the Addition of FDG-PET to the Standard Pre-operative Work up of Pancreatic Cancer Change Management − a Prospective Study

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Background: Patients with resectable pancreatic ampullary and distal bile duct (PAB) carcinomas are candidates for surgery with curative intent. Following surgery the majority of patients relapse and die of their disease. Improved patient selection is desirable. Small series have suggested that positron emission tomography with 2-Fluoro-2-deoxy-D-glucose (PET) improves detection of metastases and helps avoid futile surgery in up to 15% of patients. We prospectively evaluated the impact of the addition of PET to the standard work up of PAB carcinomas.
Materials and Methods: Prospective single-arm single institution study. Included patients had suspected or proven resectable PAB carcinoma. Resectability was determined by standard imaging and multi-disciplinary team discussion. Following this, patients underwent PET scan. The primary outcome was to determine the percentage of patients in whom there was a change in management plan due to PET.
Results: To date 33 patients have been recruited, 31 with PAB (84% pancreas, 13% distal bile duct, 3% ampulla), 2 with benign pathology. Median age 63 (range 35−84), 76% male. The sensitivity of PET for the primary carcinoma was 61%. PET changed the management in 3 of the 31 patients with carcinoma (9.7%, 95% CI 2.0% to 25.8%). In these 3 patients PET detected metastases not demonstrated on prior imaging (liver 2, retroperitoneal node 1). In 3 further patients PET failed to detect metastases; in 2 patients metastases were detected intraoperatively (liver 1, peritoneum 1), and in one patient non-FDG-avid liver lesions rapidly progressed post-pancreaticoduodenectomy. In 5 patients the carcinoma was unresectable at laparotomy due to local invasion. PET did not detect this or change management in any of these patients. Twelve patients had locoregional node metastases in the resection specimen, none of which were FDG-avid. In 6 patients (18%) PET detected independent pathology; 3 patients required additional investigations − skin biopsy (squamous cell cancer), axillary biopsy (benign), colonoscopy (tubular adenoma).
Conclusion: PET had low sensitivity for detecting the primary PAB tumours. It does not appear useful in identifying locally advanced tumours or locoregional nodes. PET can detect distant metastases not otherwise apparent resulting in a change of management in 9.7% of patients. Hence it may not be useful as a routine staging tool. Additional investigations may be initiated due to incidental abnormalities found on PET.
Trial registry number ACTRN12607000604404.

6525 POSTER

A Phase I Study of Triapine and Radiation in Patients With Locally Advanced Pancreas Cancer

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Background: Pancreas cancer is one of the leading causes of cancer death in the world. Chemoradiation provides modest improvement in outcome in locally advanced pancreas cancer (LAPCA). Triapine, an inhibitor of the M2 subunit of ribonucleotide reductase, was shown to be a potent radiosensitizer in preclinical and early clinical studies.
Materials and Methods: This is a dose escalation trial with 3 dose levels of triapine (24 mg/m^2, 48 mg/m^2, 72 mg/m^2) administered concurrently with 50.4 Gy of radiation in 28 fractions. Patients received triapine within 30 minutes of radiation on Monday, Wednesday and Friday of every other week for 5$\frac{1}{2}$ weeks. Primary endpoint was maximum tolerated dose (MTD) of triapine in combination with radiation. Secondary endpoints included response and radiographic correlates with dynamic contrast enhanced (DCE) MRI.
Results: Twelve patients were treated. Three patients were non-evaluable (NE) for the primary endpoint. Four patients (1 NE) were enrolled at dose level 1, 3 patients at dose level 2, and 5 patients (2NE) at dose level 3. The last patient is undergoing treatment at dose level 3. No DLTs have been observed. Grade 3 thrombocytopenia was seen in 1 patient at dose level 2. Two patients (18%) achieved a PR and 5 patients (45%) had SD. One patient underwent successful surgical resection after therapy. mOS is 7.5 months (range 1.3−20 months, 95% CI 3–15.8). DCE MRI was found to be a predictor for early response to therapy.
Conclusion: The combination of triapine and radiation is safe and tolerable in patients with LAPCA with evidence of promising preliminary activity. Triapine should be considered to be part of future combinatorial studies with gemcitabine or a fluoropyrimidine with radiation in LAPCA. DCE MRI is a potentially useful imaging tool to predict early response to therapy in patients with LAPCA and deserves further investigation.