4 hours after cisplatin treatment. In contrast, it was over expressed with oxaliplatin treatment at all time intervals
Conclusions: XPA and ERCC1 were over expressed with oxaliplatin treatment while in cisplatin treatment they were nearly undetectable. These findings suggest that cisplatin is more toxic in oesophageal adenocarcinoma cells than oxaliplatin.

3516 POSTER

Report of safety analysis in a randomized phase III study comparing S-1 alone with S-1 plus CDDP in advanced gastric cancer (The SPIRITS trial. TS-1 Advanced Gastric Cancer Clinical Trial Group)

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Background: The oral fluoropyrimidine S-1 (TS-1®) is based on the biochemical modulation of 5-fluorouracil, and is widely used as a single agent and in combination therapies for advanced gastric cancer (AGC) in Japan. A phase III study comparing S-1 alone with S-1 plus CDDP was conducted to evaluate the efficacy and feasibility of the S-1 plus CDDP combination as first-line therapy of AGC in Japan. Its result will be presented at ASCO 2007 as oral presentation. Analysis of safety and continuity will be presented at ECCO.
Material and Methods: Patients (Pts) were randomized to one of two treatment arms by multicenter. Arm S: S-1 was administered orally 40 mg/m^2 twice daily for 28 days, followed by 14 days rest as one cycle. Arm SP: S-1 was administered orally 40 mg/m^2 twice daily for 21 days followed by 14 days rest, while CDDP was administered intravenously 60 mg/m^2 on day 8 as one cycle. Pts were required to have unresectable/recurrent AGC. Primary endpoint was overall survival (OS). Secondary endpoints were RR, time to treatment failure (TTF) and toxicity.
Results: 305 pts (Arm S/SP, 152/153) were randomized between Mar 2002 and Nov 2004. The eligible pts were 299 (Arm S/SP, 150/149). The MST of Arm S/SP were 335.5 days (95% CI: 292–402)/396.0 days (95% CI: 342–471), respectively. The OS for Arm SP was superior to Arm S (log-rank p = 0.0366, hazard ratio: 0.774, 95% CI: 0.608−0.985). RR of Arm S/SP was 31.1%/54.0%. Median TTF of Arm S/SP were 119.0 days (95% CI: 91–136)/145.0 days (95% CI: 112–162). Pts received a median of 3.0 cycles (range, 1−12) for Arm S and 4.0 cycles (range, 1−11) for Arm SP of chemotherapy. The percentage of compliance for Arm S in 4th cycle and Arm SP in 5th cycle was 92.4% and 76.1%. The most common reason of study-off was progression of disease in both arms. The overall percentage of grade 3/4 toxicity was 24.7% (Arm S) and 66.9% (Arm SP). Grade 3/4 toxicities that occurred more than 10% with one of both arms were leucopenia (Arm S/SP: 2.0%/11.5%), neutropenia (Arm S/SP: 10.7%/39.9%), Hb decreased (Arm S/SP: 4.0%/25.7%), anorexia (Arm S/SP: 6.0%/30.4%) and nausea (Arm S/SP: 1.3%/11.5%). Treatments related death was not observed in this study.
Conclusions: It could be regarded that combination therapy of S-1 plus CDDP is useful, which does not have any problem in continuity and compliance. Accordingly, the combination therapy was active and well tolerated as one of the first line standard treatment of AGC.

3517 POSTER

The novel biomarker (HOXB2) predicts response to pancreatectomy for pancreatic cancer

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A current challenge in the treatment of cancer is identifying biomarkers of response to therapies in order to tailor optimum treatment to individual patients. Pancreatic Cancer (PC) is the fourth leading cause of cancer death in Western societies with a 5-year survival rate of less than 10%. Pancreatectomy is the only therapeutic intervention that offers the chance of long term survival, however, only 10 to 20% of patients who undergo pancreatectomy survive >3 years with prognostic factors only determined after pathological examination of the resected specimen. Identification of a biomarker of response to surgical resection that can be determined preoperatively offers the potential to significantly improve survival and quality of life for patients with PC by improving patient selection for pancreatectomy.
We examined the aberrant expression of over 20 genes identified using transcript profiling or known to be important in carcinogenesis using immunohistochemistry and in-situ hybridisation in a cohort of 124 patients with pancreatic cancer to identify potential biomarkers of prognosis and response to operative resection.
Aberrant expression of p53, p21WAF1/CIP1, p27KIP1, p16INK4A, cyclin D1, cyclin E, DPC4/Smad4, EGFR, beta-catenin, sfrp4, HER2, LMO4, HOXB2, c-myc, LRAT, S100P, S100A6, S100A2, RAI3 and CRBP1 were identified in a significant proportion of PC. Multivariate analysis of clinicopathological variables (tumor size, differentiation, subtype, lymph node metastases, perineural invasion and vascular space invasion), treatment parameters (margin involvement, adjuvant therapy, resection type), and aberrant expression of the above candidate biomarkers identified that HOXB2 expression and resection margin involvement by tumor were the only 2 independent prognostic factors. Patients who had absent HOXB2 expression and had clear margins after pancreaticoduodenectomy (48%) had an actual survival of 42% at 3 years and 21% at 5 years, compared to those with HOXB2 expression and/or positive surgical margins who had all died by 28 months.
HOXB2 expression may represent a surrogate marker of advanced disease, can potentially be assessed preoperatively using FNAB, and is currently the best predictor of outcome and response to operative resection to be reported. Preoperative assessment of HOXB2 expression has potential clinical utility in predicting response to operative resection for PC to allow better selection of patients for operative intervention.

3518 POSTER

Cetuximab with Irinotecan/FA/5-FU as first-line treatment in advanced gastric cancer: Preliminary results of a non-randomized multicenter AIO phase II study

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Background: Since cetuximab had promising activity in irinotecan-based therapies in colorectal cancer and irinotecan has shown to be effective with 5-FU/FA in advanced or metastatic gastric cancer, we evaluated tolerability and efficacy of cetuximab with irinotecan/5-FU/FA as first-line treatment in patients with unresectable locally advanced or metastatic gastric cancer.
Methods: Patients (pts) with previously untreated adenocarcinoma of stomach, the esophagogastric junction or distal esophagus, with an ECOG Performance status (PS) < 2, measurable lesions and adequate organ functions were eligible. Pts received cetuximab at an initial dose of 400 mg/m^2 followed by weekly 250 mg/m^2 over 60 min, irinotecan 80 mg/m^2 over 90 min and sodium folinate 200 mg/m^2 plus 5-FU 1500 mg/m^2 over 24 hours on days 1, 8, 15, 22, 29 and 36 (one week rest). Cycles were repeated on day 50. Treatment was continued until disease progression. Tumor assessments were performed every other cycle, i.e. every 14 weeks.
Results: From August 2006 – April 2007, 41 of 50 enrolled pts were included into a preliminary analysis: 75.6% were males, median age 63 years (range 35−77); median PS 0 (70.7%); 66% had gastric and 34% had esophagogastric or Barrett carcinomas. The median treatment duration was 7 weeks (range 0−28). Common grade 3/4 toxicities were diarrhoea 7.3%, skin toxicities 7.3%, leucopenia 4.9%; other serious adverse events seen in 1 patient were non-fatal lung embolism, acute coronary syndrome and hypersensitivity reaction to cetuximab, respectively. Among 20 evaluable patients, complete or partial remissions were seen in 45% and tumor control (remission or stable disease) was obtained in 85%. No early death occurred.
Conclusion: Cetuximab combined with irinotecan/FA/5-FU can be safely administered and is effective in advanced gastric cancer. Updated results will be presented at the meeting.