2%/2%; gastrointestinal perforation 1%/1%; pulmonary embolism 2%/2%; deep vein thrombosis 1%/2%; cerebrovascular accident 0.3%/0.3%; proteinuria 1%/0%. Thyroid-stimulating hormone levels were obtained in 217 pts; of 197 pts with normal baseline values, elevations $\geqslant 5\,\mu U/mL$ occurred in 36%/8% of pts.
Conclusion: The addition of A to G does not increase survival in pts with advanced PC.

6503 ORAL

Gemcitabine with or without prophylactic weight-adjusted dalteparin in patients with advanced or metastatic pancreatic cancer (APC): a multicentre, randomised phase IIB trial (the UK FRAGEM study)

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Background: The incidence of vascular thromboembolism (VTE) in advanced pancreatic cancer (APC) is high (17−30%) and has been shown to confer a worse prognosis. Direct mortality and morbidity related to VTE may be an underlying cause. Nullifying VTE therefore could have beneficial effects for APC patients. The study hypothesis is that the use of weight-adjusted dalteparin dosing (WAD) in a primary prophylaxis setting may eliminate VTE to an extent that survival benefit may be seen.
Methods: Patients, aged 18 years or older, with histologically/cytologically-confirmed APC, Karnofsky performance status KPS 60–100, with adequate haematological, hepatic and renal function, no baseline VTE, no hemorrhagic risk, no recent VTE (<6 months) and not on anticoagulants were randomised to either gemcitabine 1000 mg/m^2 (Burris schedule) (Arm A) or same with WAD (CLOT schedule) for 3 months (Arm B) stratified by extent of disease (LA vs. M), and KPS (90–100 vs. 80−60). Primary end point was the reduction of all-type VTE and lethal VTE during study period (<100 days). ('FRAGEM', EUDRACT No:111–111111−11, Sponsored by Hull and East Yorkshire NHS Trust-University of Hull).
Results: From April 2003 to January 2009, 123 (A/B 64/59) pts were randomised from 6 institutions in the UK. Pre-planned analysis of the primary endpoint of overall reduction of VTE and reduction of VTE during WAD treatment period <100 days) is presented. Overall VTE was 31% (A) Vs 12% (B) ($p = 0.019$) with RR = 0.38 (95% CI = 0.17, 0.84). VTE during treatment period (<100 days from randomization): 25% (A) vs. 3.5% (B) ($p = 0.002$) with RR = 0.14 (95% CI 0.03, 0.58). Secondary endpoints, lethal VTE and sudden death were seen only in (A) 9%Vs 0% (B) ($p = 0.028$) RR = 0.08 (95% CI = 0.005, 1.45) and Early Death Burden was 11% (A) vs. 7% (B) ($p = 0.62$). Analysis of VTE profile and results of other secondary endpoints (toxicity, OS and TTF) will be presented at the meeting.
Conclusions: This is the only study to have looked at WAD-dosing in this setting and one of the largest studies of Low molecular weight anticoagulant prophylaxis in APC. It demonstrates a significant reduction in overall VTE and a highly significant reduction of VTE during WAD-prophylaxis with a reduction of lethal VTEs/sudden death. This trial suggests that prophylaxis with WAD over 3 months at least, is beneficial for APC patients receiving gemcitabine and should be considered a new standard of care.

6504 ORAL

Survial advantage for irinotecan versus best supportive care (BSC) as 2nd-line chemotherapy in gastric cancer – a randomized phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO)

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Background: Up to now the value of 2nd-line therapy for metastatic gastric cancer is unclear. So far there are no randomized phase III data comparing 2nd-line chemotherapy to BSC. Irinotecan has proven activity in 1st-line therapy. In this randomized phase III study we compared irinotecan to BSC to evaluate the value of 2nd-line chemotherapy for gastric cancer.
Methods: Prospective multicenter randomized phase III study, open label. *Eligibility:* Metastatic or locally advanced gastro-esophageal junction or gastric adenocarcinoma. Objective tumor progession (PD) within 6 months after 1st-line chemotherapy. ECOG PS 0−2. *Statistics:* Primary endpoint: Overall survival (OS). Hypothesis: H1: OS (Irinotecan) >OS (BSC). Calculated number of pts needed (power 80%, alpha error 5%): 60 pts per arm. Stratification for (a) PD less versus (vs) more than 3 months after 1st line chemotherapy, (b) ECOG PS 0/1 vs 2. *Treatment*: Arm A: Irinotecan 250 mg/m^2 q3w (1st cycle) to be increased to 350 mg/m^2, depending on toxicity. Arm B: BSC.
Results: Between Oct 2002 and Dec 2006 40 pts were randomized. The study was closed prematurely due to poor accrual. Arm A:21 pts, arm B 19 pts. Median age A: 58 yrs (43−73), B: 55 yrs (35−72); PD less vs more than 3 months after 1st-line chemotherapy: A: 18/3, B: 17/2 pts. ECOG PS 0/1 vs 2: A: 17/4, B: 14/5 pts. Pre-treatment with cisplatin: A: 21, B:19 pts. *Arm A:* 68 cycles administered in 21 pts. *Toxicity*: (main CTC grade 3/4): Nausea 1 pt, vomiting 1 pt, diarrhoea: 5 pts, neutropenic fever: 2 pts, data incomplete 6 pts. In 37% of 19 evaluable pts irinotecan dose was escalated to 350 mg/m^2. *Response* (19 pts evaluable): No objective responses, SD 58%, PD 42%. Improvement of tumor related symptoms: 44% of pts in arm A, 5% in arm B.
Survival: (all 40 pts evaluable): median survival arm A: 123 days (95%CI 95–216), arm B 73 days (95%CI 53–149); OS: HR = 0.48 (95%CI 0.25−0.92), Logrank test (two-sided): $p = 0.023$. In univariate analyses for potential prognostic markers treatment with irinotecan had the most significant impact on survival.
Conclusion: To our knowledge this is the first randomized phase III study investigating 2nd-line chemotherapy in gastric cancer. Irinotecan as 2nd-line chemotherapy significantly prolongs overall survival compared to BSC. 2nd-line chemotherapy can now be considered as a proven option in gastric cancer.

6505 ORAL

A randomised phase II trial of a drug eluting bead in the treatment of hepatocellular carcinoma by transcatheter arterial chemoembolization

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Background: A widely accepted transarterial chemoembolization (TACE) regimen includes administration of doxorubicin-in-oil emulsion followed by gelatine sponge particles. Recently, a drug eluting bead (DEB) has been developed to enhance drug delivery to the tumor and reduce systemic availability. Purpose of this randomized trial was to compare conventional TACE with DEB-TACE for the treatment of intermediate-stage HCC.
Methods: 212 patients (185 males, 27 females; mean age, 67 years) with Child-Pugh A-B cirrhosis and large and/or multinodular HCC were randomized to receive DEB (DC Bead; Biocompatibles, UK) loaded with doxorubicin or conventional TACE. Randomization was stratified according to Child-Pugh class, performance status, bilobar disease (yes or no) and prior curative treatment (yes or no). Tumor response at 6 months was the primary endpoint.
Results: DEB-TACE showed a higher rate of complete response, objective response and disease control compared with conventional TACE (27% vs 22%; 52% vs 44%; and 63% vs 52% respectively, $P > 0.05$). Patients with Child-Pugh B, ECOG 1, bilobar disease and recurrence following curative treatment showed a significant increase in objective response ($p = 0.038$) compared to the control. There was a marked reduction in serious liver toxicity in patients treated with DEB-TACE. The rate of doxorubicin-related side effects was significantly lower ($p = 0.0001$) in the DEB-TACE group compared with conventional TACE group.
Conclusion: DEB-TACE with doxorubicin is safe and effective in the treatment of intermediate-stage HCC and offers a significant benefit to patients with more advanced disease.