Gastro-intestinal malignancies

Oral presentations (Wed, 23 Sep, 09:00−10:45)

Gastro-intestinal malignancies − Non-colorectal cancer

6500 ORAL

Gemcitabine with or without cisplatin in patients (pts) with advanced or metastatic biliary tract cancer (ABC): final results of the UK ABC-02 trial

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Background: There is no established standard chemotherapy for pts with inoperable ABC. We previously reported an improvement in progression-free survival (PFS) in a randomised phase II trial of 86 pts (ABC-01) using gemcitabine/cisplatin (GemCis) *vs.* gemcitabine (Gem) (Valle ASCO-GI 2006, abstr. 98). This study was extended into ABC-02, a phase III trial, to recruit a further 314 pts with overall survival (OS) as the primary end-point.
Methods: Consenting pts with histologically/cytologically-confirmed ABC, aged ⩾18 years, ECOG performance status 0−2, and adequate haemato-logical, hepatic and renal function were randomised to receive either Cis (25 mg/m^2) followed by Gem (1000 mg/m^2 D1, 8 q21 d) for 8 cycles, or Gem alone (1000 mg/m^2 on D1, 8, 15 q28 d) for 6 cycles, stratified by extent of disease, site of primary tumour, ECOG score and centre. The trial had an 80% power to detect an OS hazard ratio of 0.73.
Results: From May 2005 to October 2008, 324 pts were randomised to ABC-02 from 34 UK centres. We report the pre-planned combined analysis of ABC-01 and ABC-02 based on 410 pts (GemCis = 206/Gem = 204). Patient characteristics: median age 64 yrs (range 23−85); male (47%); metastatic disease (75%), locally advanced (25%); gallbladder (36%), bile duct (59%), ampulla (5%); and ECOG 0−1 (87%), 2 (12%). With a median follow-up of 6.1 months and 263 deaths, the median OS was greater with GemCis than Gem, 11.7 vs. 8.2 months (log rank p = 0.002), with hazard ratio 0.68 (95%-CI 0.53, 0.86). The median PFS was greater with GemCis than Gem, 8.5 vs. 6.5 months (log rank p = 0.003), with hazard ratio 0.70 (95%-CI 0.56, 0.88). Toxicity was similar between the arms (by week 12, 57% had a grade 3/4 toxicity in each arm), though there was a slight excess of neutropenia using GemCis. We will present CA19.9 and Quality of life data.
Conclusions: This study demonstrates a clear survival advantage for GemCis in ABC without added clinically significant toxicity. We will present updated and final survival, CA19.9 and QL data.

6501 ORAL

Sunitinib (SU) vs placebo for treatment of progressive, well-differentiated pancreatic islet cell tumours: results of a phase III, randomised, double-blind trial

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Background: Limited treatment options exist for advanced pancreatic islet cell tumours (neuroendocrine carcinoma of the pancreas) and most have not been tested in rigorous randomised controlled trials. SU has shown activity in patients with pancreatic islet cell tumours in a phase II study. This multinational phase III trial (NCT00428597, sponsored by Pfizer Inc) assessed SU efficacy and safety in patients with progressive growth of pancreatic islet cell tumours.
Methods: Patients enrolled had local, locally advanced or metastatic, well-differentiated pancreatic islet cell tumours not amenable to curative therapy, and disease progression in the past 12 months. Patients were randomised to placebo or SU 37.5 mg/day continuous daily dosing, with best supportive care. Progression-free survival (PFS) was the primary endpoint; the study was powered to detect a 50% improvement in PFS with a target sample size of 340 patients. Safety and tolerability were assessed.
Results: From Jun 2007 to Feb 2009, patients were randomised to SU (n = 75) or placebo (n = 79). Median age was 56 years (range 25−78); 27% ⩾65 years old; 53% female. Further demographic and treatment history data are being analysed. The most frequently reported all-cause, all-grade adverse events (AEs) with SU were diarrhoea (63%), nausea (53%), vomiting (39%), asthenia (35%) and fatigue (35%). The most frequent Grade 3/4 AEs included neutropenia (SU vs placebo, 12.3% vs 0%), hypertension (8.8% vs 0%), abdominal pain (7.0% vs 10.4%), diarrhoea (7.0% vs 1.5%), hypoglycaemia (7.0% vs 3.0%), and palmar–plantar erythrodysaesthesia (7.0% vs 0%). At interim analysis (73 events evaluated, including 63 due to disease progression), median PFS was 11.1 months in the SU arm vs 5.5 months with placebo (hazard ratio for progression, 0.397 in favour of SU; 95% CI 0.243, 0.649; 2-sided p value <0.001). The study was stopped early as recommended by an independent Data Monitoring Committee; patients in the placebo arm were able to cross over to SU. Analysis of survival is ongoing; 5 deaths occurred in the SU arm and 15 in the placebo arm.
Conclusions: SU prolonged PFS compared with placebo in patients with progressive well-differentiated pancreatic islet cell tumours, with an acceptable safety profile. Analysis of data is ongoing; additional data will be presented as available. These data contribute to a growing body of evidence indicating SU activity in patients with advanced pancreatic islet cell tumours.

6502 ORAL

A double-blinded, placebo-controlled, randomized, phase III study of axitinib (AG-013736; A) plus gemcitabine (G) vs. G plus placebo (P) in advanced pancreatic cancer (PC) patients (pts)

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Background: A is an oral, potent, selective inhibitor of vascular endothelial growth factor receptors 1, 2, 3. In a randomized, phase II trial of G +/− A in PC pts, there was a non-statistically significant gain in overall survival (OS) in pts treated with A+G compared with G (6.9 vs. 5.6 months; Spano et al. *Lancet* 2008). These data led to an international, double-blind, placebo-controlled, randomized, phase III trial of A+G vs. P+G in advanced PC pts (NCT00219557; Sponsor: Pfizer Oncology).
Material and Methods: Eligible pts had no prior chemotherapy, ECOG performance status (PS) 0/1, no tumor invasion of adjacent organs, no recent thrombosis, and no bleeding risk. Primary endpoint: OS. Stratification: disease extent (locally advanced vs. metastatic). Statistics: 90% power to detect a death hazard ratio of ⩽0.73 for G+A with a 1-sided 0.025 false-positive error rate. Pts were randomized in a 1:1 ratio to receive G 1,000 mg/m^2 over 30 minutes on days 1, 8, 15, Q28 days, and either A 5 mg or P orally BID. CT scans were obtained Q8 weeks.
Results: 632 pts were enrolled from 7/07 to 10/08. At the time of the pre-specified interim analysis, data from 630 pts were available. Based on the interim analysis after 223 deaths had occurred, the Independent Data Monitoring Committee in 1/09 determined that the futility boundary had been crossed. Pts on treatment were notified and unblinded, and discontinuation of A was recommended. Pt characteristics (314 A+G/316 P+G): male 61%/60%; median age 61/62 years; PS 1 52%/49%; stage IV disease 80%/79%. Median time on treatment: 2.7/2.8 months (mo). Median follow-up: 5.6/5.6 mo. Median OS: intent-to-treat population 7.4/8.2 mo (95% CI: 6.2−9.5/6.9−10.4 mo); locally advanced disease 9.0/10.6 mo (95% CI: 7.3−10.1/9.9–not available); metastatic disease 6.9/6.9 (95% CI: 5.6−10.2/6.2−8.2). Overall death hazard ratio: 1.06 (95% CI: 0.82−1.38). Deaths as of 1/09: 112/111 pts. Of the 613 pts evaluable for toxicity, grade 3/4 toxicity included (% pts A+G/P+G): neutropenia 13%/12%; thrombocytopenia 12%/7%; anemia 3%/8%; fatigue 8%/7%; anorexia 6%/4%; hypertension 7%/2%; asthenia 6%/2%; gastrointestinal bleeding