3519 POSTER

Cost of treating advanced gastric cancer (AGC) with capecitabine/cisplatin vs. 5-FU/cisplatin regimens: An economic evaluation from an Italian perspective

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Background: A recent randomised phase III trial of capecitabine/cisplatin (XP) vs. continuous infusion of 5-FU/cisplatin (FP) as first-line therapy in patients with AGC met its primary endpoint of non-inferior progression-free survival (PFS) [Kang et al. ESMO 2006]. There was a trend toward superior efficacy with XP in terms of both PFS (median 5.6 months for XP vs. 5.0 months for FP) and response rates. An economic evaluation was conducted to compare the costs of the two regimens from an Italian perspective.
Materials and Methods: Direct medical costs during the study period were estimated from the perspective of the Italian health system. The costs of the two regimens were estimated based on the trial results on actual dose and the number of administrations, and unit costs in an Italian setting. The adverse event (AE) profiles were used to estimate the costs of treating AEs. An expert panel estimated typical treatment patterns and costs of treating major AEs. Indirect costs for time and travel for study drug administration were estimated.
Results: Patients in the XP arm received 5.2 cycles of therapy vs. 4.6 cycles for patients receiving FP. The replacement of infusional 5-FU with oral capecitabine reduced the number of hospital clinic visits by 17.6 (22.8 for FP vs. 5.2 for XP). Chemotherapy drug costs were estimated to be €1200 higher in the XP arm, but drug administration costs were €2900 lower, yielding a net cost saving with XP of €1700 per patient. The AE profiles were similar: associated costs to treat major (grade 3/4) AEs were less than €170 per patient and were lower in the XP arm. As a result of the additional 17.6 visits for infusion of 5-FU, FP patients incurred substantially greater indirect costs in terms of lost time and travel expenses.
Conclusion: Oral capecitabine benefits AGC patients by reducing the number of infusion visits and time spent receiving treatment, and would produce significant direct medical cost savings in an Italian setting. AE costs are similar with the 2 regimens. Given the trend to superior efficacy, the projected direct and indirect cost savings, and the convenience of oral treatment, XP would be considered a dominant (less costly and more effective) regimen for AGC from both a health system and societal perspective.

3520 POSTER

Worldwide differences in the surgical management of gastric cancer: results of the REGATE study

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Background: The REGATE (REgistry of GAstric cancer Treatment Evaluation) registry is a multicentre, observational study involving >300 investigators in 20 countries, designed to describe the pattern of care in patients (pts) with newly diagnosed gastric cancer (GC) worldwide from 2004 to 2008.
Materials and Methods: Study centres were selected by two-level sampling, according to locally available data. Subjects aged $\geqslant$18 years with newly diagnosed primary GC were enrolled. Data were collected at the time of diagnosis and 8–10 months after the initial visit.
Results: Present results are based on first visit data from 3118 pts in 19 countries (cut-off December 2006). End of study data are available for 1893 pts (Eastern Asia, 28.1%; Latin America, 16.3%; Middle East/Africa/Indian Peninsula, 22.1%; Russia, 25.0%; Europe, 8.6%). Diagnosis was by endoscopic examination in 94.0% of pts. Primary tumour was located in the antrum in 39.7% of pts and in the gastric body in 36.7% of pts. Distribution according AJCC stage I/II, III and IV was 41.6%, 18.1% and 40.3%, respectively, based on the pts' latest available data. A lower percentage of stage IV disease was observed in Eastern Asia (36.5%) and a higher percentage in the Middle East/Africa/Indian Peninsula (54.2%). Curative surgery was planned for 67.4% of pts but actually took place in 61.8%. Among pts who did not receive curative surgery, 78.3% were AJCC stage IV. Most of these pts received palliative/non-curative therapies only (62.2%) or were not treated (31.6%). Among all pts treated with surgery $\pm$ chemotherapy, surgical interventions were: distal subtotal gastrectomy (43.2%), total gastrectomy (38.2%), pancreas-preserving splenectomy (5.6%), proximal subtotal gastrectomy (5.2%) and hemi-pancreas splenectomy (2.4%). Curative surgery without chemotherapy was more commonly used in Russia and Eastern Asia than in other countries, irrespective of AJCC stage (stage I/II, 78.5% and 74.5% vs 27.0%; stage III, 71.2% and 31.5% vs 16.8%; stage IV, 29.2% and 19.6% vs 4.0%, respectively).
Conclusions: These data indicate that, while surgery is the main curative strategy for GC worldwide, there are large geographical variations. In contrast to Europe, surgery alone without adjuvant or neoadjuvant chemotherapy is common in Russia, regardless of disease stage. In Eastern Asia, stage I/II disease is generally treated using surgery alone, with the addition of chemotherapy for stage III disease.

3521 POSTER

Prolongation of survival and improvement of performance status (PS) by chemotherapy in gastrointestinal cancer patients with poor PS

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Background: The prognosis of advanced gastrointestinal cancer patients, especially those with poor PS, is generally dismal. Needless to say, such patients are ineligible for participation in clinical studies. However, there are many patients with poor PS who wish to receive chemotherapy.
Materials and Methods: From June 2000 to February 2007, a total of 559 patients with advanced cancer, including 335 gastrointestinal cancer patients, were treated by chemotherapy in our hospital. Of these, 116 gastrointestinal cancer patients (gastric 37, colorectal 32, pancreatic 27, biliary tract 11, esophageal 9) had poor PS (ECOG PS 3: 73 patients, PS 4: 43 patients). Retrospective analysis of these 116 patients was performed.
Results: In 107 patients with at least one measurable lesion, a partial response according to RECIST criteria was obtained in 15 patients (14.0%). In 65 patients with ascites (52 patients), pleural effusion (26 patients), or both (13 patients), 12 of the patients (18.5%) achieved decreased fluid accumulation. A decline in tumor markers (>25%) was observed in 30 patients. As a result, 38 patients (32.7%, including 10 patients with PS 4) achieved a tumor response, a decrease in accumulated fluid, or a decline in tumor markers, which resulted in a survival benefit compared to the other 78 patients without effect (6.9 months vs. 2.2 months, $p < 0.001$). Improvement in PS was seen in 16 patients (13.8%). Alleviation of some symptoms was observed in 31 out of 104 symptomatic patients (29.8%). A better response and/or a decline in tumor markers significantly correlated with alleviation of symptoms and improvement of PS ($p < 0.001$). One treatment related death was seen (0.8%).
Conclusions: With regard to response rate, chemotherapy was rarely effective for patients with advanced gastrointestinal cancer with poor PS. However, more than a few patients gained a certain survival benefit, improvement in PS and alleviation of symptoms. Thus, chemotherapy may be warranted in cases of patients with advanced gastrointestinal cancer who wish to receive chemotherapy despite the low possibility of response.

3522 POSTER

Incidence of thromboembolic disease (TED) in gastroesophageal patients associated with chemotherapy

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Background: Upper gastrointestinal tract cancers are associated with increased incidence of TED. Chemotherapy increases this risk however, the incidence and significance of TED associated with chemotherapy in this group of malignancies is unclear. We therefore conducted this audit to determine the incidence of symptomatic and asymptomatic TED in a population of patients with gastroesophageal cancers.
Method: Data was collected from 283 sequential patients with gastroesophageal carcinoma treated in the Northern Ireland Cancer Centre over a 3 year period (2003–2005). TED was defined as arterial [cerebrovascular accident (CVA), myocardial infarction (MI), peripheral ischaemia] or venous [deep venous thrombosis (DVT), pulmonary embolism (PE)]. Diagnosis of TED was confirmed by appropriate clinical investigation.

Results: Of 283 patients reviewed, 173 (61.1%) patients had oesophageal cancer while the remaining had gastric carcinoma. TED was detected in 31 (10.9%) patients overall. The incidence of TED was the same in both oesophageal and gastric cancer patients. TED was: PE 10, DVT 15 (9 related to indwelling venous catheter), IHD 3 and CVA 3. 19.3% of patients with TED presented with clinically occult TED (3 DVT and 3 PE) detected on imaging. All patients who developed TED received platinum-based chemotherapy and this accounts for 12% of patients who received platinum-based chemotherapy for the above period. None of the 4 patients who received irinotecan combination chemotherapy developed TED. 64.5% of patients were subsequently hospitalised following TED diagnosis with no TED-specific mortality.
Conclusions: Our observations suggest TED is a frequent complication of chemotherapy for gastroesophageal cancer patients. The majority of patients are symptomatic, however with improved imaging technology such as use of multidetector CT scanning occult TED may increasingly be detected. The potential use of antiangiogenic agents with conventional cytotoxic chemotherapy may increase the incidence further. If these observations are confirmed in larger prospective cohort studies, thromboprophylaxis may be justified, however may be difficult due to the risk of GI bleeding in these patients.

3523 POSTER

Glufosfamide (GLU) plus gemcitabine (GEM) in pancreatic adenocarcinoma: results of a Phase 2 trial

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Background: Glufosfamide is glucose linked to isophosphoramide mustard, the active metabolite of ifosfamide. Cancer cells use glucose at a higher rate than normal cells, which may lead to preferential metabolic targeting by GLU. The Phase 1 study established a GLU dose of 4500 mg/m^2 for the GLU + GEM regimen. The objectives of the Phase 2 part of this study were to evaluate the safety and efficacy of GLU+GEM in pts with pancreatic adenocarcinoma.
Materials and Methods: Eligible pts had metastatic and/or locally advanced pancreatic adenocarcinoma previously untreated with chemotherapy, Karnofsky Performance Status $\geqslant$70, creatinine clearance (CrCL) $\geqslant$60 mL/min and acceptable hematologic and liver function. Pts received GLU 4500 mg/m^2 iv over 4 hours on Day 1 and GEM 1000 mg/m^2 iv over 30 minutes on Days 1, 8 and 15 of every 28-day cycle. CT scans were done every 8 weeks. Primary endpoint was response rate.
Results: Twenty-nine pts were enrolled. One patient with ineligible histology was excluded from efficacy analyses. The 14 male/15 female pts had a median age of 59 years. Twenty-three pts had distant metastases; 6 pts had locally advanced disease. Median cycles on treatment was 4 (range 1−14+). Eight pts completed all 6 cycles including 5 pts with stable or responding disease who continued on study for additional cycles. Six of 28 (21%; 95% CI: 8−41%) pts had a partial response (duration 1.0+ to 9.7+ months) one unconfirmed. Eleven of 28 (39%) pts had stable disease (median duration 5.3 months). Median progression-free and overall survival were 3.7 and 6.0 months. Six-month survival was 50% (95% CI: 35−72%). Grade 3 and 4 neutropenia occurred in 9 (31%) and 13 (45%) pts. Grade 3 and 4 thrombocytopenia occurred in 7 (24%) and 1 (3%) pts. Five pts (18%) had a GLU-related serious adverse event (SAE); renal tubular acidosis (RTA) with renal failure (2 pts), RTA, vomiting, nausea. Three pts died from SAE unrelated to GLU. Another pt developed renal failure after hypotension associated with pulmonary embolus. The CrCL fell below 60 mL/min in 10 of 27 (37%) pts with CrCL $\geqslant$ 60 at baseline. Median change in CrCL from baseline to last measurement was −6 mL/min.
Conclusions: These data indicate that GLU + GEM may benefit pts with chemotherapy naive pancreatic adenocarcinoma. Hematologic and renal toxicity may be more than would be expected with either agent alone. No unanticipated adverse events based on previous experience with glufosfamide were observed.

3524 POSTER

High rate of clinical benefit response in patients with advanced biliary tract cancer receiving gemcitabine plus capecitabine. A prospective, multicenter phase II trial of the Swiss Group for Clinical Cancer Research (SAKK 44/02)

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Background: In phase II trials, several chemotherapy regimens have yielded tumor response rates of 20−30% with survival times between 7−12 months in patients (pts) with advanced biliary tract cancer. However, no information is available on patient-reported outcomes in this group. As primary objective we evaluated the association of palliative chemotherapy with tumor-related symptoms measured using clinical benefit response parameters [Burris et al., J Clin Oncol 1997].
Materials and Methods: Previously untreated pts with pathologically confirmed, locally advanced, unresectable or metastatic biliary tract cancer were recruited. Pts had to be symptomatic of biliary tract cancer and have at least one of the following at baseline: Karnofsky performance status (KPS) between 60 and 80, and/or average baseline analgesic consumption $\geqslant$10 mg morphine equivalents per day, and/or average pain intensity score of $\geqslant$20 mm (based on a visual-analogue scale). Treatment consisted of gemcitabine 1 g/m^2 IV on days 1 & 8 with capecitabine 650 mg/m^2 orally BID on days 1−14 of a 3 week cycle for a maximum of 8 cycles. The primary endpoint was the number of pts categorized as clinical benefit responders (CBR) or stable CBR (SCBR) on all of the clinical benefit parameters (pain intensity, analgesic consumption, KPS and weight) determined on the basis of the first 3 cycles. Secondary endpoints were clinical benefit rate in all cycles, tumor response (RECIST), adverse events, quality of life, time to progression (TTP) and overall survival (OS).
Results: Between May 2003 and June 2006, 44 pts were enrolled (8 with gallbladder cancers, 36 with bile duct cancer) in 6 centers. Median age was 65 years. A total of 266 cycles were administered (median 8) with an overall relative dose intensity of 90%. Main grade 3/4 adverse events included: neutropenia (39%), anemia (2%), thrombocytopenia (7%), fatigue (11%), nausea (5%), constipation (5%), vomiting (2%) and diarrhea (2%). After 3 cycles, 16 pts (36%) achieved a CBR and 15 pts (34%) achieved a SCBR. Over the full course of treatment, 25 pts (57%) achieved a CBR and 8 pts (18%) a SCBR. We observed 1 CR (2%), 10 PRs (23%) and 24 SDs (55%). Median TTP and OS were 7.2 months and 14.2 months, respectively.
Conclusions: Combination chemotherapy with gemcitabine plus capecitabine is well tolerated, effective and leads to a high number of CBR. CBR can be used to evaluate the impact of palliative chemotherapies in pts with biliary cancer.

3525 POSTER

Low dose sequential multi-drug regimens for the elderly and the resistant advanced pancreatic cancer patients.

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Background: The GFLIP regimen was designed based on human ex vivo sensitivity tests performed on a series of de novo pancreatic tumors, which identifed multiple drug interactions optimum at low drug concentrations. The regimen provides conditions for these drug interactions to occur simultaneously and overcome the individual tumors heterogeneous resistance to many drug combinations.
Methods: Pts with unresectable, metastatic and recurrent pancreatic cancer were treated with a low dose q2wk version of GFLIP using cisplatin 40 mg/m^2 with or without subsequent addition of low dose docetaxel 25−35 mg/m^2 on failure of GFLIP. Pts with PS 4, atypical cystic pathology, apocrine or endocrine tumors and Ro staus were excluded from analyses. Eligibility allowed prior treatment with the test drugs. Cohorts of consecutively accrued pts provided 185 prospectively registered pts for intent to treat analyses of overall survival, plus age, stage, prior therapy and