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Phase III randomised comparison of gemcitabine (GEM) versus gemcitabine plus capecitabine (GEM–CAP) in patients with advanced pancreatic cancer

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Background: Both gemcitabine and fluoropyrimidines are valuable treatment for advanced pancreatic cancer. This study was designed to compare the survival of gemcitabine (GEM) with gemcitabine plus capecitabine (GEM-CAP).

Methods: Patients with previously untreated histological or cytological proven locally advanced/metastatic carcinoma of the pancreas and performance status $\leqslant 2$ were recruited. Patients were randomised to GEM (1000 mg/m^2 weekly $\times 7$ q8 weeks, then 1 week rest, thereafter weekly $\times 3$ q4 weeks) or to GEM–CAP (gemcitabine 1000 mg/m^2 weekly $\times 3$ q4 weeks and capecitabine 1660 mg/m^2/day for 21 days followed by 7 days' rest). Treatment continued until disease progression or intolerable toxicities. The primary outcome measure was survival.

Results: Between May 02 and Jan 05, 533 patients were randomised to GEM (n = 266) and GEM–CAP (n = 267) arms. Baseline characteristics were well balanced (GEM/GEM–CAP) with regards to median age (62/62), stage IVB disease (71%/70%) and WHO performance status (PS) 0–1 (82%/81%). At the time of this interim analysis in May 05, 373 (70%) deaths have occurred. GEM–CAP significantly improved overall survival over GEM alone (Hazard Ratio [HR]: 0.80; 95%CI: 0.65–0.98; p = 0.026). The median survival for GEM and GEM–CAP was 6 months and 7.4 months respectively and 1-year survival rates were 19% and 26% respectively. After adjusting for baseline stratification factors (disease extent and PS), the survival advantage for GEM–CAP remains (HR: 0.77; 95%CI: 0.63–0.95; p = 0.014). The objective response rates were 7% (0CR, 19PRs) and 14% (3CRs, 35 PRs) in GEM and GEM–CAP respectively (p = 0.008). Grades 3/4 toxicity episodes in GEM and GEM–CAP arms respectively were anaemia (2%/1%), neutropenia (11%/17%), thrombocytopenia (2%/3%), fever (1%/0%), diarrhoea (1%/1%), stomatitis (0%/0%), hand–foot syndrome (0%/2%) and vomiting (2%/1%).

Conclusions: With 70% death having occurred, these data show a significant improvement in overall survival by the addition of capecitabine to gemcitabine over gemcitabine alone in advanced pancreatic cancer with acceptable levels of toxicity.