progression and toxicity. Pts were randomized to GEM 1000 mg/m^2 iv d 1+8 and CAP 650 mg/m^2 po q 12 hrs d 1–14 every 3 w or GEM 1000 mg/m^2 weekly x7, 1 w rest and then weekly x3 q4w. Trt continued for 6 mo or until progression. The study was designed to detect an increase of median survival from 5 to 7 months. CB was evaluated based on changes in pain/pain medication, KPS and weight during a period >4 weeks. The trial was independently monitored.
Results: From 7/01 to 6/04 319 pts from 30 institutions in 8 countries were randomized. 79% had metast. disease, 67% required pain medication and 53% had KPS of ⩾90. The median OS was 8.4 mo for GEMCAP and 7.3 mo for GEM (p = 0.314). 89% of all patients have died. Confirmed response rates were 10.1% vs. 7.9%, median duration of response 7.4 vs. 5.9 mo and median TTP 4.8 vs. 4.0 mo for GEMCAP and GEM resp. A multivariate Cox regression of OS on strat. factors and trt revealed that in pts with KPS ⩾90 those treated with GEMCAP had a significantly higher median OS of 10.1 vs 7.5 mo (p = 0.033). 111 pts (73%) with GEMCAP and 121 pts (82%) with GEM were at least 4 weeks on study trt and evaluable for CB.
Conclusions: An update on CBR and other QoL parameters in relation to clinical outcome will be presented.
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Results of a phase II study with sunitinib malate (SU11248) in patients (pts) with advanced neuroendocrine tumours (NETs)

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Background: NETs are characterised by an indolent course and are often resistant to standard cytotoxic chemotherapy. These tumours are highly vascular with both carcinoid tumours and pancreatic (islet cell) NETs expressing high levels of VEGF and VEGFR. Sunitinib malate is an oral multitargeted tyrosine kinase inhibitor that specifically inhibits VEGFR, PDGFR, KIT, RET and FLT3, and has shown activity in pts with NETs included in phase I trials.
Patients and methods: Pts (n = 109) with advanced unresectable NETs (43 carcinoid, 66 islet cell) received sunitinib 50 mg/day po for 4 weeks followed by 2 weeks off treatment. Cycles were repeated every 6 weeks. Prior chemotherapy was allowed and pts receiving octreotide could continue with treatment on study. In addition to response, survival and adverse events, quality of life was measured (EQ-5D and FACIT-Fatigue subscale) and correlative safety/efficacy analyses were undertaken using both sunitinib plasma levels and NET biomarkers.
Results: Data are available for 102 pts (median no. of cycles: 5, range 1–14; median dose intensity 93%) with the following characteristics: median age: 57 yrs (range 32–81), M/F (%) 59/41, ECOG PS 0/1 (%) 54/43. The most common (>2%) grade 3/4 treatment-related adverse events (AEs) (%) included fatigue (25/0), neutropenia (12/4), thrombocytopenia (8/0), hypertension (8/0), vomiting (6/0), nausea (60), diarrhoea (5/0), dehydration (4/0), mucosal inflammation (3/0), anorexia (3/0) and glossodynia (3/0). Discontinuations due to AEs were reported for 7% of pts.
Best objective tumour response rates defined by RESIST were (n = 102): partial response (PR) 9 pts (9%); stable disease (SD) 84 (82%) and progressive disease (PD) 4 (4%). Best response according to tumour type is shown. Median time to tumour response was 16 weeks and median time to tumour progression was 40 weeks (carcinoid = 42 weeks; islet cell = 33 weeks). Results from analyses investigating correlation between NET biomarkers and treatment-related outcomes are pending.

	PR**	SD	PD	Not evaluable
Islet cell* (n = 61)	8 (13%) 95% CI 5.8–24.2	46 (75%)	4 (7%)	3 (5%)
Carcinoid* (n = 41)	1 (2%) 95% CI 0.1–12.9	38 (93%)	0 (0%)	2 (5%)

* Patients with baseline and at least 1 subsequent imaging assessment **Confirmed response by investigator (at least two assessments)

Conclusions: Sunitinib shows single-agent clinical activity in pts with advanced unresectable NETs and is associated with acceptable adverse events that result rarely in treatment discontinuation.

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Randomized, multicenter, phase 3 study of 1st-line irinotecan + 5FU/folinic acid vs cisplatin + 5FU in patients with advanced gastric cancer – quality of life analysis

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Background: An open-label, multicenter study of 1st-line advanced gastric cancer pts was designed to compare the effects of CPT-11 + 5FU/FA with CDDP + 5FU. Primary efficacy variable: time to progression (TTP); secondary endpoints: time to treatment failure (TTF), overall survival (OS), global health status/QOL scale, and safety.
Methods: Male and female pts aged 28–77 y were randomized to receive CPT-11 80 mg/m^2 iv as 30-min infusion, then FA 500 mg/m^2 iv over 2 h, and then 5FU 2000 mg/m^2 iv over 22 h weekly for 6 wk (IF); or CDDP 100 mg/m^2 iv as 1–3 h infusion on day 1, and then 5FU 1000 mg/m^2/d continuous infusion over 5 d every 4 wk (CF). Treatment was administered up to progression, unacceptable toxicity, or consent withdrawal.
Results: Of 337 randomized pts, 333 (170 in IF; 163 in CF) were treated. In the full-analysis population, a trend toward superiority was noted for TTP with IF vs CF (HR 1.23; 95% CI 0.97–1.57, P = 0.088) corresponding to a 19% progression in risk reduction. Median TTP for IF vs CF: 5.0 vs 4.2 mo; median TTF: 4.0 (3.6–4.8) vs 3.4 (2.5–3.8) mo (HR 1.43; 95% CI 1.14–1.78; P = 0.018). There was no difference in OS. Although there were no significant differences between summary measures of postbaseline global health status/QOL, there was a trend toward significance for the maximum and mean measures favoring IF. Mean summary measures for several secondary QOL endpoints showed significantly better results for IF vs CF, eg, physical functioning (P < 0.005), nausea/vomiting (P < 0.05), and Euroqol 5-Dimension thermometer (P < 0.005) and health utility index (P < 0.05). 67 pts (40%) in IF had grade 3/4 drug-related AEs vs 73 (44%) in CF. IF pts had more grade 3/4 drug-related diarrhea (21.6% vs 7.2%); CF pts had more grade 3/4 neutropenia (52% vs 25%), febrile neutropenia or neutropenic infection (10.2% vs 4.8%), stomatitis (16.9% vs 2.4%), and nausea (9.0% vs 4.8%). CF pts had more hematologic and renal toxicities. More pts withdrew from the study due to drug-related AEs with CF than with IF (21.5% vs 10.0%; P = 0.004), including 5 toxic deaths with CF vs 1 with IF.
Conclusions: In advanced gastric cancer pts, IF showed a trend towards TTP superiority vs CF. IF demonstrated significant improvement in several QOL scales vs CF, as well as a better safety profile. Thus, CPT-11 + 5FU/FA is a safe alternative 1st-line treatment option without CDDP for advanced gastric cancer and may be useful in treating pts with poor performance status.

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An intensive weekly chemotherapeutic regimen with 5fluorouracil, leucovorin, cisplatin and epidoxorubicin (PELFw) as adjuvant treatment in high-risk radically resected gastric cancer patients: results of a randomised controlled trial

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PELFw showed significant benefit in metastatic and locally advanced gastric cancer (J Clin Oncol 1997, Br J cancer 2004). This trial was designed to determine whether this effect translates into a survival advantage in high-risk radically resected gastric cancer patients.
From January 1998 to January 2003, 400 patients with stage pT3 N0 and pT2,3 N1,2,3, were randomised to receive PELFw, 8 weekly administration of cisplatin 40 mg/m^2, leucovorin 250 mg/m^2, epidoxorubicin 35 mg/m^2, 5fluorouracil 500 mg/m^2, glutathione 1.500 mg/m^2; lenograstin was administered daily for 6 days every 7at the dose of 6 μg/Kg, or