confirms that infusional 5-FU/FA plus IRI should be considered as a reference treatment in metastatic CRC.

1089 ORAL

Improved safety of capecitabine vs bolus 5-FU/leucovorin (LV) as adjuvant therapy for colon cancer (the X-ACT phase III study)

M. Nowacki[1], H. Kröning[2], A. Cervantes[3], F. Husseini[4], J. McKendrick[5], J. Schuller[6], C. Twelves[7], A. Wong[8], J. Zaluski[9], J.-Y. Douillard[10]. [1]*The Maria Sklodowska-Curie Memorial Cancer Center, Warsaw, Poland;* [2]*Städtisches Klinikum, Magdeburg, Germany;* [3]*Hospital Clinico, Valencia, Spain;* [4]*Hôpitaux Civils, Colmar, France;* [5]*Box Hill Hospital, Box Hill, Australia;* [6]*Krankenanstalt Rudolfstiftung, Vienna, Austria;* [7]*Beatson Oncology Centre, Glasgow, UK;* [8]*Tom Baker Cancer Centre, Calgary, Canada;* [9]*Greatpoland Cancer Center, Poznan, Poland;* [10]*Centre René Gauducheau, Nantes, France*

Background: tumor-activated capecitabine (X) produced significantly superior response rates and equivalent progression-free and overall survival compared to bolus 5-FU/LV (Mayo clinic regimen, M), with an improved safety profile and fewer hospitalizations in 1st-line metastatic colorectal cancer (n=1207 patients). This high activity, improved safety and patient preference for oral chemotherapy led us to move X forward into the adjuvant setting and compare it to the current global standard, M.

Materials and methods: patients with fully resected Dukes' C colon carcinoma were assigned to oral X (8 cycles of 1250 mg/m^2 twice daily days 1-14, every 3 weeks) or i.v. M (6 cycles of LV 20 mg/m^2 + 5-FU 425 mg/m^2 days I-5, every 4 weeks) for 24 weeks.

Results: a total of 1987 patients from 162 centers in 25 countries were randomised between 11/98 and 11/01. The arms were well balanced for median age (years) [range]: X 60.4 [25-80], M 61.0 [22-82]; ECOG score (% 0/1): X 86/14, M 86/14; sex (% Male/Female): X 54/46, M 54/46; and nodal status (% N1/N2): X 69/30, M 71/29. Overall, 81% of X patients received all 8 cycles and 87% of M patients received all 6 cycles. The most common, related, clinical adverse events (AEs, ≥15% all grades) are presented in the table. X consistently caused less all grade nausea/vomiting, diarrhea, stomatitis and neutropenia, across all age groups (<60, 60-70, >70). X caused less grade 3-4 stomatitis (X 2%, M 15%) and neutropenia (X 2%, M 26%) but more grade 3 hand-foot syndrome (X 18%, M <1%). Grade 3-4 diarrhea (X 12%, M 13%), nausea/vomiting (X 3%, M 3%) and fatigue (X <1%, M 1%) were comparable. Dose reductions for AEs were similar in incidence (X 40%, M 44%) with second dose reduction less common with X (13%), than with M (26%). All-cause, 60-day mortality was X 5 (0.5%) and M 4 (0.4%). Treatment-related deaths were X 3 (0.3%) and M 4 (0.4%).

	Capecitabine (Xeloda®) n=996 All grades (%)	Mayo n=973 All grades (%)	P value
Diarrhea	46	64	<0.001
Nausea/ Vomiting	36	51	<0.001
Stomatitis	22	61	<0.001
Neutropenia	32	63	<0.001
Fatigue/ Asthenia	23	23	0.98
Alopecia	6	22	<0.001
Hand-foot syndrome	61	10	<0.001

Conclusion: in the adjuvant setting oral X has an improved safety profile vs i.v. M, with less diarrhea, nausea/vomiting, stomatitis and alopecia, as seen in metastatic disease. Efficacy data are expected in 2004 after 632 events and if positive would suggest an important role for capecitabine in adjuvant therapy, given these encouraging results and the known patient preference for oral chemotherapy.

1090 ORAL

Continuation of irinotecan (CPT-11) beyond 8 cycles does not improve outcome in patients with advanced colorectal cancer resistant to fluoropyrimidines: results of a phase III multi-centre randomised trial

J.L.B. Dickson[1], K.R. Lal[1], A.R. Norman[1], P.J. Ross[1], J. Oates[1], A. Massey[1], M.E. Hill[2], G. Middleton[3], C. Topham[3], D. Cunningham[1]. [1]*The Royal Marsden Hospital, Dept. of Medicine, Sutton, United Kingdom;* [2]*Kent Oncology Centre, Dept. of Medical Oncology, Maidstone, United Kingdom;* [3]*Royal Surrey County Hospital, Dept. of Medical Oncology, Guilford, United Kingdom*

Background: Irinotecan (CPT-11) given until disease progression (PD) is an accepted standard therapy for advanced colorectal cancer (CRC) resistant to fluoropyrimidines.

Purpose: To determine whether continuation of CPT-11 beyond 8 cycles improves outcome.

Patients and Methods: Patients (pts) with locally advanced or metastatic CRC and radiological evidence of PD within 24 weeks of completion of fluoropyrimidines were eligible. Pts may have received previous adjuvant chemotherapy and a maximum of 3 lines of palliative chemotherapy. All pts were treated with CPT-11 350 mg/m2 IV over 30 minutes, 3 weekly for 8 cycles, and those with disease response or stabilisation were then randomised to continuation until PD or best supportive care (BSC).

Results: Between 11/97 and 12/02, 333 pts were recruited, of whom 55 pts (16.5%) achieved disease response or stabilisation and underwent randomisation. 230 pts (69%) developed PD, 30 pts withdrew with toxicity, 2 pts refused randomisation and continued CPT-11, and 2 pts were withdrawn. The mean age of randomised pts was 62.4 years (range 42-78). Patient demographics between the 2 arms were well matched. 25 pts, including 6 responders, continued CPT-11 and a total of 277 further cycles were delivered; the median number of cycles delivered was 12 (range 9-20). No further responses were observed after randomisation. The only grade 3/4 toxicity observed was diarrhoea (8%). 30 pts, including 8 responders, were randomised to BSC with 1 remaining in CR. 16 pts with PD received further chemotherapy, of whom 8 received further CPT-11. No difference in progression-free survival (PFS) was observed at 6 months (36.4% for the CPT-11 continuation arm, 95% CI 17.4-55.7 vs 25% for the BSC arm, 95% CI 34.2-71.4; p=0.999). There was no difference in overall survival at 1 year (46.3% for the CPT-11 continuation arm, 95% CI 25.1-65.1 vs 54.8% for the BSC arm, 95% CI 34.2-71.4; p=0.11). No differences in mean global quality of life scores 12 weeks after randomisation were seen (p=0.446).

Conclusion: Continuation of CPT-11 beyond 8 cycles in the small group of patients with disease response or stabilisation does not improve PFS nor OS, nor does it result in significant additional toxicity, or further deterioration in quality of life.

1091 ORAL

How to explain the improvement in survival for colorectal cancer? A French population-based study

E. Mitry[1,2], A.M. Bouvier[1], J. Estève[3], J. Faivre[1]. [1]*Registre des tumeurs digestives, INSERM EPI106, Dijon, France;* [2]*CHU Ambroise Paré - APHP, Fédération des spécialités digestives, Boulogne, France;* [3]*CH Lyon-Sud, Laboratoire de biostatistique et modélisation en épidémiologie, Pierre Bénite, France*

Population-based statistics indicate that colorectal cancer survival has improved over the past 20 years. Little is known about the reasons of this trend. We have previously reported the important role of operative mortality reduction (Mitry et al. Br J Surg 2002; 89:1557-62). The purpose of this work was to study trends in colorectal survival over a 24-year period and to understand the reasons of the improvement in survival beyond the reduction of operative mortality.

Patients et methods: A series of 5,874 cases of colorectal cancers diagnosed between 1976 and 1999 in a well-defined French population were included. Trends in relative survival were estimated.

Results: The dramatic decrease in operative mortality after surgery for cure did not explain all the improvement in survival: after exclusion of operative mortality, the 5-year relative survival rate increased from 49.2 to 56.3 per cent between the 1976-87 and 1988-99 periods (50.3 and 58.0 (p<0.001) in patients under 75 and 47.1 and 53.6 per cent (p<0.001) in patients 75 and over, respectively). Trends were different between age groups. In patients 75 and over there was an increase in the proportion of patients resected for cure from 57.5% (1976-87) to 77.9% (1988-99) associated with an overall improvement in stage at diagnosis. Survival after surgery for cure as well as stage specific survival remained stable indicating that the improvement in survival was in relation with the increase proportion of patients resected for cure. In patients under 75, the increase of patients resected for cure was not the only explanation since there was also an improvement in survival after surgery for cure (from 64.9% to 72.7%, p=0.003) mainly because of the improvement in prognosis of stage III tumours (from 35.7% to 48.6%, p = 0.001). Five-year relative survival did not significantly change for advanced tumours but a significant improvement was observed for 1- and 2-year relative survival in patients under 75.

Conclusion: Trends in survival are very different between age groups. The improvement seen in overall survival for older patients can be attributed to the increase in the proportion of patients resected for cure. For younger patients, there was an increase in the proportion of patients operated for cure but also an improvement in stage-specific survival for stage III tumours suggesting a role for adjuvant chemotherapy. Progress in palliative