dose of irradiation boost (HDRT) are studied in a 4 arms trial (A= ICT, B=ICT+HDRT, C= Reference= Pelvic RT: 45 Gy in 25 fractions with 2 cycles of 5FU-CDDP W1 and W5 and a boost of 15 Gy, D= HDRT). The aim of the study (closed in March 2005, 307 pts included) was to compare the results of the 101 first pts and to assess by an IRC the absence of deleterious effect or initially unpredictable difference between the 4 arms and to confirm the number of pts to be included.

Materials and methods: 101 pts included by 20 institutes in 29 months were analysed. The age was 59 years [range 31–81], the sex ratio was 6/1. All the LAACC were SCC histologic type. There were 3 T1, 55 T2, 22 T3, 20 T4, 1 TX, 57 N0, 18 N1, 24 N2–3, 2 NX. The T size was <4 cm in 26 pts and ⩾4 cm in 69 pts, ND 6 pts. The 4 arms were well balanced concerning the sex ratio, age, stage, T size, differentiation.

Results: One violation of the protocol was noticed (metastatic disease). The tolerance to the treatment was similar in the 4 arms (3 toxic deaths, 4 pts did not receive the irradiation boost). A CTC grade 3–4 toxicity was described 27, 33, 23, 19 times in the arms A, B C, D, respectively. The compliance to the treatment was: 99% for ICT, 100% for pelvic RT-CT (median dose= 45 Gy), and 96% for the boost. The tumour complete (and partial) responses at 2 months were: A: 84% (96%), B: 90% (100%), C: = 78% (87%), D: = 78% (100%), (NS).

The median follow-up was 36 months [1–62]. Overall local failures were 23%: arm A: 32%, arm B: 9.%, arm C: 27%, arm D: 19%. The actuarial results at 3 years were:

Local control (82.5%): arm A: 71%, B: 95%, C: 80%, D: 88%.

Event free survival (74%): arm A: 73%, B: 76%, C:71%, D:65%.

Overall survival was 78%. The causes of the 24 deaths were the cancer in 16 pts (A: 7 pts, B: 1 pt, C: 4 pts, D: 4 pts), 3 treatment related deaths, and 3 intercurrent deaths. The actuarial colostomy free survival was 82% at 2 years: A: 74%, B: 85%, C: 88%, D: 84%.

Conclusion: This intermediate analysis assessed the good tolerance of the intensification of the treatment of LAACC by an ICT and a HDRT. The absence of deleterious effect or unexpected significant improvement by the intensification of the treatment confirmed the necessity to include more than 300 pts, to be able to obtain a significant difference.

615 POSTER

Safety, tolerability and efficacy of the addition of bevacizumab to oxaliplatin/fluoropyrimidine regimens as first-line treatment of metastatic colorectal cancer (mCRC): Results of TREE 2 cohort of the TREE study

H. Hochster[1], L. Hart[2], R.K. Ramanathan[3], J. Hainsworth[4], S. Griffing[5], R. Mass[5], Y. Nagarwala[6], G. Jirau-Lucca[6], A. Shpilsky[6], B.H. Childs[6].
[1]NYU Cancer Institute, Medical Oncology/Clinical Pharmacology, New York, USA; [2]Florida Cancer Specialists, Medical Oncology, Fort Myers, USA; [3]University of Pittsburgh Cancer Center, Medical Oncology, Pittsburgh, USA; [4]Sarah Cannon Cancer Center, Medical Oncology, Nashville, USA; [5]Genentech, Inc, Oncology, South San Francisco, USA; [6]Sanofi-Aventis, Oncology, Bridgewater, USA

Background: The addition of bevacizumab (Bev) to fluorouracil (FU)-based combination chemotherapy results in statistically significant improvement in survival among patients (pts) with metastatic colorectal cancer *(Hurwitz H et al. NEJM 2004; 350:2335–2342)*. The TREE study was designed to assess the safety, tolerability and efficacy of each of three oxaliplatin (OX) plus fluoropyrimidine (FP) regimens (bolus (b), infusional or oral FP; in the TREE-2 cohort, Bev 2.5 mg/kg/week was added to each regimen.

Materials and methods: Eligibility: age ⩾18; measurable untreated mCRC; PS = 0–1. **Primary endpoint**: Grade 3–4 toxicities in the first 12 weeks of treatment; **Secondary endpoints**: RR, TTP, and OS. The regimens in mg/m^2 were: m**FOLFOX+Bev** = O 85, Leucovorin (LV) 350 mg, 5FU bolus 400 & 2400 CIV x 46 hrs and Bev 5 mg/kg q 2 wk; **bFOL+ Bev** = O 85 days (d) 1&15, LV 20 & bolus 5FU 500 d 1, 8, 15 q 4 wk and Bev 5 mg/kg q 2 wk; **CapOx+Bev** = O 130 d 1, Capecitabine 850 x 14d and Bev 7.5 mg/kg q 3 wk.

Results: 223 pts were randomized; 213 were treated. Selected grade 3–4 toxicity during first 12 weeks of treatment is shown in the table. To date, the major reason for discontinuation in each arm has been development of adverse events (AE), but the time to discontinuation appears to be comparable to other clinical trials utilizing similar OX-containing regimens. Confirmed overall RR in treated patients was: **mFOLFOX+Bev** 52%, **bFOL+Bev** 34%, **CapOx+Bev** 45%. 49% of pts would be censored at this point, 5% of pts are still on study treatment; accordingly, corresponding TTP data are not yet mature, which may be a sign of potential prolongation of TTP due to addition of Bev vs. non-Bev regimens.

Conclusions: Treatment with Bev + mFOLFOX is tolerable, with a promising RR in this patient population, particularly as compared to the TREE-1 cohort (Proc ASCO GI, 2005). Grade 3–4 toxicity with first line Bev plus OX based chemotherapy is less than that reported with Bev + IFL. All regimens of FP administration are active in combination with Bev but mFOLFOX appears to have the best balance of response and toxicity. We await additional confirmation of efficacy as determined by median TTP.

Events	mFOLFOX-Bev N = 71 (%)	bFOL-Bev N = 70 (%)	CapeOx-Bev N = 72 (%)
Vomiting	1	11	7
Dehydration	6	11	8
Diarrhea	10	26	17
Neutropenia	35	13	4
Febrile neutropenia	3	1	0
Hand–foot syndrome	0	0	7
Neurotoxicity	3	4	7
Hypertension	9	4	10
Bleeding	0	4	1
Thrombosis (arterial)	0	0	1
Proteinuria	0	0	1
Any Grade 3 or 4	65	60	58

616 POSTER

Safety analysis of first-line bevacizumab plus chemotherapy in patients with metastatic colorectal cancer (mCRC) participating in a US registry

M. Kozloff[1], A. Cohn[2], N. Christiansen[3], P. Flynn[4], F. Kabbinavar[5], R. Robles[6], M. Ulcickas-Yood[7], S. Sarkar[8], J. Hambleton[8], A. Grothey[9].
[1]Ingalls Hospital, Harvey, IL, USA; [2]Rocky Mountain Cancer Centers, Denver, CO, USA; [3]South Carolina Oncology Associates, PA, Columbus, SC, USA; [4]Park Nicollet Clinic Cancer Center, St Louis Park, MN, USA; [5]UCLA School of Medicine, Los Angeles, CA, USA; [6]Bay Area Cancer Research Group, Concord, CA, USA; [7]EpiSource, LLC, Hamden, CT, USA; [8]Genentech Inc, South San Francisco, CA, USA; [9]Mayo Clinic, Rochester, MN, USA

Purpose: Data showing that bevacizumab (BV) increases overall survival when used first line in combination with 5-FU/LV +/– irinotecan to treat mCRC [Hurwitz et al. NEJM 2004; 22: 2335–42; Mass et al. JCO 2004; 22 (July 15 Suppl): abstract 3616] led to US approval early in 2004. Data indicate that certain serious adverse events, including GI perforations, occur rarely but more frequently in patients treated with BV + chemotherapy (CT) than those who receive CT alone. The US FDA has approved bevacizumab for use with all 5-FU-based CT regimens, including FOLFIRI and FOLFOX. A surveillance registry (BRiTE) was opened after US regulatory approval to evaluate safety in clinical practice.

Methods: BRiTE was opened in February 2004. Planned enrolment is 2,000 patients with mCRC receiving first-line BV + CT. Choice of CT regimen is at physician discretion. Eligibility criteria were minimised to promote enrolment of a broad mCRC population. Data on history of hypertension, stroke or myocardial infarction, diabetes, hypercholesterolemia, atrial fibrillation, chronic anticoagulant or aspirin use, peptic ulcer disease, diverticulosis, and recent surgery or endoscopy are collected at baseline. Patients are followed for up to 3 years. Clinical data (including survival, disease progression and adverse events) are collected every 3 months.

Results: As of March 2004, 1367 patients (median age 63 [range 22–92]; PS 0–1 85.5%; primary colon cancer 80.1%) had been enrolled at 273 US sites. The most common first-line CT regimens used with BV are FOLFOX (49.8%), FOLFIRI (15.0%), IFL (11.9%) and bolus 5FU/LV (7.8%). 541 patients have had a 3-month assessment and 420 a 6-month assessment. Among the 1367 patients enrolled, BV-related serious adverse events have been reported in 110 patients (8.0% of enrolled patients). These include 22 GI perforations (1.6%) and 7 post-operative hemorrhages or wound-healing complications (0.5%); other reported events include venous (2.0%) and arterial (0.4%) thromboembolic events.

Conclusions: In patients with mCRC treated with BV in combination with various CT regimens, the safety profile of BV appears to be consistent with that observed in clinical trials, suggesting that it is feasible to combine BV with regimens such as FOLFIRI and FOLFOX. The latter combination has recently been shown to improve survival in a phase III study [Giantonio et al. JCO 2005:23 (June 1 Suppl): Abstract 2]. Recruitment will close on June 30, 2005; updated data will be presented.