oxaliplatin (100 mg/m^2)/raltitrexed (2.5 mg/m^2) on day 1, and 5-FU (800 mg/m^2)/folinic acid (250 mg/m^2) on day 2 during pelvic RT (45 Gy). BEV (5 mg/kg) was given biweekly 4 days before beginning of CT/RT for 2 courses. Toxicity was graded with NCI-CTC v.3. PR was defined using Mandard tumor regression grade (TRG). According to the Simon's two-stage design, assuming an hypothesis of a 50% TRG1 (complete tumor regression) (α error = 0.05, β error = 0.20), at least 6/16 TRG1 should be obtained to continue accrual to 46 pts. CECs and TLG were evaluated at baseline (BL) on day 10 and before surgery, by flow cytometry and FDG-PET, respectively. Statistical analysis was by Mann-Whitney test.

Results: We obtained 23 TRG1 (50%), 14 TRG2 (30%) and 8 TRG3-4 (17%). Grade ¾ neutropenia was the most common adverse event (13/46 pts, 28%). TLG reduction on day 10 vs BL was significantly higher in responders TRG1-2 compared to non-responders TRG3-4 pts (median -72%, range -90% + 31% vs -38%, range -45% + 25%; $p < 0.05$). Median CECs at BL were higher in TRG1-2 vs TRG3-4 pts (median 0.22/µl, range 0-3.98 vs 0/µl, range 0-0.174; $p = 0.009$). Moreover, in TRG1-2 pts CECs were significantly reduced on day 10 vs BL (median 0.014/µl, range 0-2.29; $p = 0.002$). This pattern was not seen in TRG3-4 pts with a tendency toward increased levels (median 0.316/µl, range 0-2.64; $p = 0.097$). In both TRG 1-2 and TRG 3-4 preoperative CECs and PET-CT studies were not predictive of PR.

Conclusions: Current scheme of BEV plus CT and RT appears safe and active, yielding high rate of TRG1 and TRG2 responses in pLARC. Early FDG-PET and CECs evaluation emerged as potential biomarkers for treatment selection to be incorporated in design of future studies with this regimen. CEP and citochine data will be provided at the meeting.

Disclosure: All authors have declared no conflicts of interest.

568P SAFETY AND EFFICACY OF INTRAVENOUS CETUXIMAB (CET) AND HEPATIC ARTERY INFUSION OF IRINOTECAN, 5-FLUOROURACIL AND OXALIPLATIN IN PATIENTS WITH UNRESECTABLE LIVER METASTASES FROM WT KRAS COLORECTAL CANCER (CRC): RESULTS FROM OPTILIV EUROPEAN PHASE II TRIAL

F. Levi[1], V. Boige[2], P. Rougier[3], M. Hebbar[4], D. Smith[5], C. Focan[6], R. Guimbaud[7], C. Carvalho[8], M. Bouchahda[1], M. Ducreux[2]

[1]Chronotherapy Unit, Medical Oncology Department, Inserm, U776, Paul Brousse Hospital, Villejuif, FRANCE, [2]Oncologie Digestive, Institut de Cancérologie Gustave Roussy, Villejuif, FRANCE, [3]Digestive Oncology, Hopital European George Pompidou, Paris, FRANCE, [4]Department: Unité D'oncologie Médicale, CHRU de Lille - Hôpital Huriez, Lille, FRANCE, [5]Oncologie Digestive, Hôpital Saint André, Bordeaux, FRANCE, [6]Département D'oncologie, CHC-Clinique Saint-Joseph, Liege, BELGIUM, [7]Oncologie Médicale, CHU Toulouse Purpan, Toulouse Cedex, FRANCE, [8]Unidade de Oncologia, Hospital Prof. Doutor Fernando Fonseca, Amadora, PORTUGAL

Background: Hepatic artery infusion (HAI) of chronomodulated (Chrono) irinotecan (I), 5-Fluorouracil (F) and oxaliplatin (O), or flat O combined with intravenous (iv) F-Leucovorin allowed secondary metastases resections and prolonged survival in patients (pts) with CRC liver metastases despite prior failure of iv chemotherapy (Bouchahda, Cancer 2009; Goere, Ann Surg 2010).

Purpose: To prospectively evaluate safety and efficacy of combining iv Cet with HAI of IFO in pts with CRC liver metastases.

Methods: This Phase II trial involved pretreated pts with unresectable CRC liver metastases receiving iv Cet (500 mg/m^2) and Chrono or Conventional (Conv) HAI of I (180 mg/m^2), F (2800 mg/m^2), and O (85 mg/m^2) q2 weeks. Liver metastases were resected whenever adequately downstaged.

Results: Accrual of 64 pts (42 M, 22F; age, 33-76 years; 4 ongoing) was complete at 9 centers (4 countries) on 13/03/2012. In 62 monitored pts: PS 0/1/2 (61/36/3%), bilobar liver lesions (84%), a median of 9 metastases (1-50; largest diameter, 54 mm; range, 15-172) involving a median of 6 segments (1-8). Pts received one (44%), two (30%) or three (26%) prior iv chemotherapy lines. A median of 5 courses (1-13) was given to 59 pts (Chrono, 18; Conv, 41; 3 never treated), with artery occlusion as main cause of withdrawal (53%). Main grade 3-4 toxicities per pt were neutropenia (39%), abdominal pain (25%), fatigue (17%), diarrhea (15%), and nausea (10%). Grade 3 sensory neuropathy occurred in 3% of the pts. Intent-to-treat objective tumor response rate was 45% [95% CL,31-59], including 2 radiological complete responses. Disease control rate was 83%. Per-protocol secondary liver surgery rate was 33.3% [20.4-46.2]. One pt had pathologic complete response in 24/25 metastases in all liver segments (1-6 cm) and has been disease-free for 25+ months and alive at 38+ months. Median progression-free survival (41 events) was 9.1 months [6.5-11.6]. Preliminary median survival (19 events) is 28.6 months [16.3-40.9].

Conclusions: The combination of intravenous cetuximab with triplet HAI chemotherapy offers a safe and highly effective treatment option for patients with chemotherapy- refractory CRC liver metastases. Support: ARTBC International, Villejuif; Merck-Serono & Pfizer (France).

Disclosure: All authors have declared no conflicts of interest.

569P SOMORE TRIAL: COMBINING SORAFENIB (SOR) WITH CAPECITABINE (CAP) YIELDS HIGHLY ENCOURAGING SURVIVAL RESULTS AND ELEVATED METABOLIC RESPONSE RATE IN CHEMOREFRACTORY METASTATIC COLORECTAL CANCER (MCRC)

A. Deleporte[1], A. Hendlisz[1], T. Delaunoit[2], R. Marechal[3], M. Peeters[4], S. Holbrechts[5], M. van den Eynde[6], G. Houbiers[7], M. Moreau[8], P. Flamen[9]

[1]Medical Oncology, Institut Jules Bordet, Brussels, BELGIUM, [2]Gastroenterology, Entité Jolimontoise, La Louviere, BELGIUM, [3]Service Médico-Chirurgical de Gastroentérologie, Hopital Universitaire Erasme, Brussels, BELGIUM, [4]Medical Oncology, Universitair Ziekenhuis Antwerpen, Antwerpen, BELGIUM, [5]Medical Oncology, Hopital Ambroise Pare, Mons, BELGIUM, [6]Medical Oncology, Cliniques universitaires St-Luc, Brussels, BELGIUM, [7]Gastroenterology, Hopital Saint Joseph, Liege, BELGIUM, [8]Data Center, Institut Jules Bordet, Brussels, BELGIUM, [9]Nuclear Medicine, Institut Jules Bordet, Brussels, BELGIUM

Background: Several phases I and II trials including mCRC and metastatic breast cancer patients have suggested an interesting clinical activity in solid tumors with a SOR-CAP combination. SoMore's aim is to assess its potential benefit in chemorefractory mCRC and the predictive value of early metabolic response (MR) on survival.

Methods: SoMore (EUDRACT 2010-023695-91) is a multicentric phase II in PS 0-1 chemorefractory mCRC pts. Two co-primary objectives were defined 1) to demonstrate that overall survival (OS) at 6 months is > 30% (67 pts needed to have 90% power to detect a true rate of 50% at 1-sided level 2.5%); 2) to compare OS between early PET responders and non responders (62 deaths required before analysis -on pts assessable for MR- to detect a true HR < 0.385, assuming a 67% rate of early responders). Pts received a 1st cycle of SOR (600mg/day) CAP (1700 mg/m^2/day, day 1-14 every 21 days), then subsequent cycles with a SOR dose of 800mg/day until progression or unacceptable toxicity. FDGPET-CT was performed at baseline and before second cycle. Investigator-independent centralized PET analysis was carried out with metabolic non response defined by < 15% FDG uptake decrease in a dominant proportion (≥50%) of predefined target lesions (SUVmax> 2.5 liver uptake; size > 15 mm).

Results: Between February and October 2011, 92 eligible pts were recruited in 6 centers: 50 male pts (54%), ECOG PS 0/1 : 51 (55%)/41 (45%), median age of 61 years. A median of 5 treatment cycles were given (0-18 + , treatment ongoing in 11 pts). No toxic death was observed. Grade III-IV toxic reactions were reported in 53% of the pts, mainly fatigue (17%), hand-foot skin reaction (13%), diarrhea (13%). 3/81 pts stopped their treatment due to toxicity. OS rate at 6 months was 65/92 (71%, 95% CI : 61%-79%), significantly higher than 50% ($p < 0.001$). PET showed a MR in 65% [54%-74%] of the 79 evaluable pts. Data are not yet mature to analyze the predictive value of PET on survival.

Conclusions: SoMore largely met one of its primary objectives with an observed 71% OS at 6 months for this heavily pretreated mCRC population with manageable toxicity. Data about PET assessment according to mOS and PFS will likely be mature at the time of the meeting and presented if available.

Disclosure: All authors have declared no conflicts of interest.

570P EFFECT OF POST-PROTOCOL ANTI-EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) MONOCLONAL ANTIBODY (MAB) THERAPY ON SURVIVAL OUTCOMES IN PATIENTS WITH WILD-TYPE (WT) KRAS METASTATIC COLORECTAL CANCER (MCRC) TREATED WITH PANITUMUMAB (PMAB) PLUS CHEMOTHERAPY

J-Y. Douillard[1], M. Peeters[2], A. Rong[3], S. Siena[4], S. Braun[5], R. Sidhu[3], T. Price[6]

[1]Centre René Gauducheau, Nantes, FRANCE, [2]University Hospital Antwerp, Antwerp, BELGIUM, [3]Amgen Inc., Thousand Oaks, CA, UNITED STATES OF AMERICA, [4]Ospedale Niguarda Ca' Granda, Milan, ITALY, [5]Amgen GmbH, Zug, Switzerland, [6]Queen Elizabeth Hospital and University of Adelaide, Woodville, AUSTRALIA

Background: Results from two randomized, multi-centre, phase III studies of pmab plus chemotherapy (FOLFOX4 in 1st-line [PRIME]; FOLFIRI in 2nd-line [181]) demonstrated a trend toward improved overall survival (OS) in the experimental arms vs chemotherapy alone, analysing the ITT populations. We evaluated the hypothesis that crossover to post-protocol anti-EGFR mAb-containing therapy in the control arms may have attenuated OS outcomes.

Methods: For this retrospective analysis, we used data of both PRIME and 181 study final analyses prespecified to occur at 30 months after the last patient was enrolled. We conducted sensitivity analyses to estimate OS outcomes using statistical procedures: (1) estimating the effect of randomized treatment as if no patients in the chemotherapy arm received subsequent anti-EGFR mAb-containing therapy[a]; (2) identifying the survival differences that would have been observed had all patients stayed on protocol treatment[b]; (3) modifying the Cox proportional-Hazards model, allowing for a time-dependent covariate with value 0