placed in 54 Patients (Pts) with isolated colorectal liver metastases (CLM).

The first group (30 Pts) received intra-arterial therapy with 5-FU 600 mg/sm plus Folinic Acid (FA) 100 mg/sm at a dose previously calculated to achieve both high-dose regional therapy and adequate systemic levels; the second group (24 Pts) was treated with a regimen combining intrahepatic 5-FU 750 mg plus EPI 40 mg by 1/2-hour infusion every two weeks alternately, and bolus systemic infusion consisted of 5-FU 600 mg/sm plus FA 100 mg/sm.

Methods: (Group A) 30 Pts (21 male, 9 female; median age 62 yrs "range 46–84"; median Karnofsky-Index 80 "range 60–100"; 24 pts previously untreated with chemoteraphy) received bolus hepatic arterial infusion consisted of 5-FU and FA for once a week; there were 986 administrations. (Group B) 24 pts (16 male, 8 female; median age 54 yrs "range 31–69"; median Karnofsky-Index 80% "range 60–100"; 19 pts previously untreated with chemotherapy) received intraarterially 5-FU plus EPI every two weeks alternately, and bolus systemic infusion consisted of 5-FU and FA, there were 897 administrations. Efficacy and toxicity were regularly evaluated by clinical investigation, CT scan, X-ray, and tomografy according to WHO criteria. Survival analysis (Kaplan-Meier) was used to predict median survival and time to progression. The treatment was administered on an outpatient basis until progression (PD) or complete response (CR).

Results: (Group A): median survival time 19.6 months (range 4–63; 95% CI 17–28 months); response rate 13.3% (CR + PR), 13% PD, 74% stable disease (SD). The median time to progression was 11 months (range 2–59+; 95% CI 7–16 months). The extrahepatic progression was 45% (13/29 Pts: only extrahepatic 11%, intra-extrahepatic 34%).

(Group B): median survival time 23.3 months (range 5–41; 95% CI 13–33 months); overall response rate 46% (11/24) with 21% (5/24) of CR and 41% (10/24) of SD. The median time to progression was 11.6 months (range 2–31; 95% CI 9–16 months). The extrahepatic progression was 58% (11/19 Pts: only extrahepatic 37%, intra-extrahepatic 21%). In both groups toxicity was absent or mild and no patient stopped treatment because of side effects.

Conclusions: HAT is an effective treatment for CLM with a moderate toxicity. More studies of combined use with systemic chemotherapy are needed to finally determine the position of this therapy in the treatment system for CLM; therefore it is necessary to conduct comparative trials versus systemic chemotherapy, using the survival time as the end-point.

252 PUBLICATION

Phase I of CPT-11 (CAMPTO®) combined with 5-FU/folinic acid (FA) nordic schedule in first line metastatic colorectal cancer (CRC)

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For 40 years, 5-FU was a standard in the treatment of CRC. Multiple schedules of administration of 5-FU have been tested Combination of 5-FU with new drugs such as CPT-11 has shown promising results in 1st line treatment. A phase I/II was conducted to determine the MTD of CPT-11 150–240 mg/m^2) day 1 combined with a fixed dose of bolus 5-FU 500 mg/m^2) followed by FA (60 mg/m^2), day 1 and 2, q 2 wk as the Nordic schedule (Glimelius, Ann Oncol 4, 1993). DLT is defined as neutropenia G 4, thrombocytopenia G 4, febrile neutropenia, G 3–4 infection and any grade 3–4 non hematological toxicity that occurred at cycle 1. Preliminary results are:

CPT-11	Nb pts	Nb cycles	DLT	Responses
150	3	23	0	2 PR
180	3	25	0	1 PR, 2 NC
210	6	22	1*	1 PR, 1 NC
240	3	3	0	too early

* *G4 Neutropenia*

At 210 mg/m^2, one DLT was reported at first cycle out of 6 patients treated. The other toxicities are mild to moderate being mainly cholinergic syndrome and diarrhea. The MTD is not reached so far. Updated results will be presented at the meeting.

253 PUBLICATION

CAMPTO® (CPT-11) combined with different schedules of bolus 5-FU in 1st line treatment of metastatic colorectal cancer

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CPT-11 as single agent has shown a significant benefit on survival compared to 5-FU, in 2nd line CRC. Moreover, CPT-11 alternating with the Mayo Clinic regimen (Van Cutsem, Ann Oncol 98) has shown very promising results in first line setting. Taking into account the wide use of 5-FU in clinical practice, either as a bolus or infusional administration, it was worthwile to assess the different combination options with CPT-11 in 1st line CRC. This trial was designed to randomly assign patients (pts) in different arms as follows: A: CPT-11 + bolus 5-FU/FA weekly (4 wk–2 wk rest, CPT-11: 125 mg/m^2; FA: 20 mg/m^2; 5-FU: 500 mg/m^2); B: CPT-11 alternating with 5-FU/FA (q 6 wks, CPT-11: 350 mg/m^2; FA: 20 mg/m^2; 5-FU: 425 mg/m^2), C: 5-FU/FA (Mayo regimen FA 20 mg/m^2, 5-FU 425 mg/m^2 bolus). Efficacy is assessed every 2 cycles (cy) and safety every cy. Quality of life is evaluated by the EORTC questionnaire (QLQ-C30). The study is ongoing and 80 patients have been treated so far with 217 cy administered. Preliminary response assessment on 34 pts showed promising results with 1 CR, 3 PR, 1 MR, 1 SD and 4 PD in Arm B. Out of 58 pts evaluable for safety so far, the tolerance is good. Updated results will be presented at the meeting.

254 PUBLICATION

Advanced colorectal cancer (ACC): Impact of chronotherapy (chrono) on patients' (pts) quality of life (QoL)

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Introduction: Chrono consist of delivering chemotherapy according to different drug timing. Differences in tissues susceptibility, drugs metabolism and pharmachocynetics have been observed for 5-fluorouracil and platinum compounds resulting in a reduction of toxicity and improvment in efficacy in ACC pts.

Purpose: To evaluate the impact of Chrono on ACC patients' QoL and relationship between toxic events, PS, response and QoL.

Methods: QoL was assessed with EORTC QLQ C30 + 3 questionnaire, administered at baseline, To, after the 3rd, T1, the 6th, T2, and the 9th, T3 course (c). Pts were treated with Chronomudulated infusion of 5-fluorouracil, folinic acid ± oxaliplatin for 5 d q 3 wks by ambulatory pumps.

Results: Patient data: 84 pts were included; mean age was 62 (25–78); M/F: 52/32; PS: 0 (44 pts); 1 (25 pts); 2–3 (15 pts); 20 patients experienced WHO Grade 0–1 has maximal toxicity vs 51 with Grade 2–3; 28 obtained a PR, 43 had SD + PD. Functionig scales mean scores (phisical, role, cognitive, emotional, social function and global physical, global health, global QoL) where high during the whole period of treatment with an improvment prevalently at T2. Global physical functioning was better at T2 vs T0 ($p < 0.05$). A constant improvement of symptom scales was observed at T2 vs T0 but not at T3. Patients in the G2–3 toxicity group at 3rd and 9th c showed QoL emotional, global physical, blobal health, global QoL functioning scales scores lower than the G0–1 group ($p < 0.05$). PS 0–1 pts showed better QLQ mean scores than PS 2–3 pts for all functioning scales at T0, at the 3rd and the 6th c of therapy ($p < 0.05$). Pts who responded to therapy had higher mean scores of global QoL then patients who were resistent to therapy at the 3rd and 9th c ($p < 0.05$).

Conclusions: QoL during chrono remained high during a 6 month period of therapy. A better QoL was observed in those pts with better prognostic factors as PS and tumor responsiveness and in those who displayed a good treatment tolerance. This seams to indicate that infusional chronotherapy has a positive impact on pts QoL.