Conclusion: Although preliminary, these results show that this combination is associated with an acceptable toxicity and clinical benefit was observed in 12/20(60%).

242 POSTER

Phase I study of Irinotecan (I), Raltitrexed (R), and 5-fluorouracil (5FU) in the treatment of metastatic colorectal cancer (MCRC) refractory to thymidylate synthase inhibitors (TSI)

R. Goel[1], J. Maroun[1], C. Cripps[1], D. Jonker[1], G. Chiritescu[1], S. Dahrouge[1], L. Douglas[2]. [1] *Ottawa Regional Cancer Centre, Medical Oncology, Ottawa, Canada;* [2] *AstraZeneca, Canada*

Background: TSI are a standard component of treatment for all patients with MCRC. There is evidence of synergetic activity between I, R and 5FU in MCRC. Objectives are to establish the dose limiting toxicity (DLT), maximum tolerated dose (MTD) and recommended doses (RD) of all 3 agents combined in patients with previously treated MCRC.

Methods: This is a prospective phase I, dose escalating study. Patients (pts) were eligible if they had received a single TSI regimen in monotherapy for metastatic disease. For cohorts (coh) 1-4, pts received fixed doses of I (300 mg/m^2) with atropine on day (D) 1 and R (2.5 mg/m^2) D2. 5FU (mg/m^2) was started at 600 IV 90 min D3, and escalated by 300 until MTD was reached. Then 5FU dose was decreased to MTD-1, and R escalated to 2.75mg/m^2.

Results: 22 pts were enrolled (5, 6, 6, 2 and 3 pts in coh 1, 2, 3, 4 and 5, respectively). 77% were males. PS was 0, 1, 2, 3 in 41%, 41%, 14% and 4%. Pts received an average of 8 cycles (range: 1-16). 20 pts are evaluable for toxicity and response (2 pts in coh 5 too early). DLTs were: febrile neutropenia (coh 3), grade (gr) 3 lethargy with gr 4 neutropenia (coh 4) and febrile neutropenia with gr 3 vomiting and nausea (coh 4). MTD for escalating 5-FU was reached in coh 4 (1500 mg/m^2). Coh 5 (R 2.75 & 5FU 1200 mg/m^2) is currently ongoing. Severity of granulocytopenia appears related to 5FU dose. Gr 3-4 was seen in 20%, 67%, 83%, and 100% in coh 1 to 4. Cholinergic symptoms were rare and mild (1 gr 3). Gastro-intestinal toxicity was not dose related. Diarrhea was frequent (90%) but usually mild to moderate (2 gr 3, coh 1&4). Nausea and vomiting (N&V) were common (80%) but usually mild to moderate and controlled with anti-emetic therapy. N or V was gr 3-4 in 3 pts (2 in coh 3, 1 in coh 4). Lethargy (gr 1-3) and anemia (gr 1-2) were also common (95% each). Gr 2-4 rises in hepatic transaminase levels were infrequent (15%) and reversible. Responses were seen in all cohorts. Objective response rate: partial response 5 (25%), stable disease 14 (70%). Median progression free and overall survival were 31 and 56 weeks, respectively.

Conclusions: Further dose escalations are not planned. If coh 5 is deemed tolerable, these doses will be recommended for further studies. Combination of R, I and 5FU is well tolerated at near maximum doses of single agents and has a promising activity level in pts previously treated with a TSI. Further evaluation of this regimen in first-line for MCRC is warranted.

243 POSTER

Preoperative chemotherapy plus concomitant radiotherapy in rectal cancer patients (pts): updated results of a phase II study

M. Scartozzi[1], E. Galizia[1], S. Antognoli[1], R. Bracci[1], F. Grillo-Ruggieri[2], G. Mantello[2], C. Marmorale[3], R. Berardi[1], S. Cascinu[1], R. Cellerino[1]. [1] *Universita'-Azienda Ospedaliera Umberto I, Ancona, Clinica Di Oncologia Medica, Ancona, Italy;* [2] *Azienda Ospedaliera Umberto I, Ancona, U.O. Radioterapia, Ancona, Italy;* [3] *Universita', Ancona, Clinica Chirurgica, Ancona, Italy*

Background: Preoperative chemo-radiotherapy proved to be an effective approach for resectable rectal cancer patients. Our study aimed to evaluate the efficacy [tumour downstaging, disease free (DFS) and overall survival (OS)] and toxicity of chemo-radiotherapy in patients with locally advanced rectal cancer.

Patients and Methods: Eligibility criteria were: stage T2-4, N0-2, M0 histologically confirmed, rectal adenocarcinoma, ECOG < 2, age > 18 yrs, adequate haematological, renal and liver function. Chemotherapy consisted of cis-platinum 60 mg/m2 (day 1 and 29) and 5-FU 1000 mg/m2/day PVI for 96 hours (day 1 to 4 and day 29 to 32). Concomitant radiotherapy was administered at a total dose of 5040 cGy with 3-4 fields box-technique (28f, 180 Cgy/day). Surgery was performed 6-8 weeks following chemoradiation. Adjuvant chemotherapy (5-FU 370 mg/ m2 bolus and folinic acid, 10 mg/m2, day 1-5, every 28 days) was administered within 60 days from surgery.

Results: Forty-one pts entered the study (M/F=32/9, median age at diagnosis 59 yrs, range 37-75). Preoperative tumour stage was: T2N0M0 in 7 (17%) pts, stage T3-4 N0M0 in 16 (38%), 16 (38%) pts were N+. In 2 further pts tumour stage could not be assessed (TxN0M0). In 25 (61%) pts tumour was located within 6 cm from the anal verge. To date all pts completed neoadjuvant therapy and 40 underwent surgery (34 pts had a low anterior resection and 6 pts had an abdominoperineal resection) and 22 (54%) pts completed adjuvant chemotherapy. We observed a pathologically confirmed tumour downstaging in 21 (51%) pts with a complete response in 8 (19,5%) cases. At a median follow-up of 24 months, 10 (24%) pts relapsed (1 pts showed local recurrence and 9 pts metastatic disease), with a DFS of 18 months and OS of 25 months. Chemo-radiotherapy related toxicity was modest (NCI grade III diarrhea in 3 pts), 1 patient died for post-surgical complications.

Conclusions: Although a longer follow-up is required for more definitive conclusions, in our experience neoadjuvant chemo-radiotherapy for rectal adenocarcinoma seemed well tolerated and effective with a high response rate (22% complete response) and satisfactory local control

244 POSTER

The conservative treatment of anal canal carcinoma

N. Raffetto[1], M. Santarelli[1], A.M. Ascolese[1], C. Caruso[1], A. Papaleo[1], R. Rossi[2], V. Tombolini[3], R. Maurizi Enrici[1]. [1] *University of Rome "La Sapienza", Radiology, Rome, Italy;* [2] *University of Rome "La Sapienza", Oncology, Rome, Italy;* [3] *University of L'Aquila, Radiation Oncology, L'Aquila, Italy*

Background: In anal canal carcinoma optimal radiotherapy doses and chemotherapy schedules are not well established.

Combined chemo-radiotherapy has better survival rates than surgery, achiving preservation of anal sphincter function in the majority of patients.

Materials and methods: Between 1989 and 2002, 60 patients with basaloid or squamous cell carcinoma of the anal canal were treated at the Department of Radiology of the University La Sapienza, Rome. Patients underwent pretreatment evaluation with clinical examination, complete blood cell count, chest radiography, transrectal sonography, anorectoscopy and anal biopsy, anorectal manometry and abdominopelvic CT or MR.

Patient population consisted of 43 females and 17 males, with a median age of 65 years. Stage was: 27 cases T1-T2 N0 (45%), 8 T3 N0 (13%), 6 T4 N0 (10%), 2 T2 N+ (5%), 10 T3 N+ (16%) and 7 T4 N+ (11%).

Thirty-nine patients (65%) received concurrent chemo-radiotherapy and 21 (35%) exclusive radiotherapy because clinical contraindications to chemotherapy.

Concurrent chemotherapy included 2 cycles of infusional 5-Fluorouracil at 1000 mg/m^2/day for 4 days in the first and last week of radiation, in addition to Mitomycin C 10 mg/m^{2}or CDDP 50-75 mg/m^{2}or CBDCA 150-200 mg/m^{2}on the first day of treatment. Combined radiotherapy consisted of external-beam pelvic irradiation to a dose of 45 and a boost of 10-15 Gy or two cycles of 23.4 Gy and a boost of 15-20 Gy. Radiotherapy alone regimen consisted of 50-60 Gy and a boost of 10-15 Gy.

Results: Complete response was observed in 12/21 (57%) patients treated with exclusive radiotherapy and in 30/39 (77%) patients treated with concurrent chemo-radiotherapy. Abdominoperineal resection was performed in 5/21 (24%) patients treated with exclusive radiotherapy and in 6/39 (15%) patients of chemo-radiotherapy group. There was a small difference in the incidence of acute toxicity (evaluated with WHO scale) in the two groups. Radiotherapy exclusive regimen caused grade II proctitis 9% of patients, grade III acute haematologic toxicity in 4% and compromising sphincter function in 4%. Combined treatment caused grade II proctitis 25% of patients, grade III acute haematologic toxicity in 10% and compromising sphincter function in 13%. Median follow up was 40 months, the 5-year overall survival was 79% in the chemo-radiotherapy group vs 62% in the exclusive radiotherapy. The 10-year overall survival for the exclusive radiotherapy and chemo-radiotherapy groups was 47.6% and 69.2% respectively.

Conclusion: Combined therapy using radiation and concurrent chemotherapy with preserving anorectal function, has replaced surgery as definitive treatment for cancer of the anal canal. Variation in radiation technique have been proposed to reduce acute and late tissue toxicity observed when high radiation doses are combined with chemotherapy.