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1305

ADJUVANT ADMINISTRATION OF SUBCUTANEOUS (SC) INTERLEUKIN-2 (RIL-2) IN PATIENTS FOLLOWING RESECTION OF RENAL CELL CARCINOMA: PRELIMINARY RESULTS OF A PILOT STUDY. *T. Olencki, R.M. Bukowski, K. Zuccaro, D. McLain, P. Elson, J. Finke, A. Novick. Cleveland Clinic Foundation, Cleveland, OH.*

Adjuvant administration of rIL-2 following resection of locally advanced (T_{3a-c} N_1 M_0) or metastatic renal cell carcinoma was investigated to determine toxicity and patient (pt) tolerance to 4 different SC rIL-2 regimens. Pts with adequate cardiovascular, renal and hepatic function who had no evidence of residual disease were treated within 3 mos of surgery. Pts. were randomized to receive rIL-2 at either 2.0 or 4.0 MIU/m² S.C. BID d1–5 q o wk (cohorts I & II respectively) or wks 1–4 every 8 wks (cohorts III & IV respectively) for a total of 24 wks. Dose reduction (50%) for ≥ Gr III toxicity or patient intolerance was permitted. 24 pts (6/cohort) will be entered, with 17 entered to date (stage III-15, stage IV-2). 15 pts are currently evaluable and preliminary results are as follows:

Cohort	No. Eval.	Completed 24 wks	Dose Reduction	Currently On Therapy
I	4/4	2	0	1
II	4/4	2	0	1
III	5/4	2	1	1
IV	4/3	1	1	2

Toxicity included constitutional symptoms in all pts and Gr III hepatic toxicity consisting of SGOT elevation (1 pt cohort IV) which subsequently returned to normal. Dose reduction or discontinuation of rIL-2 was required in 2/15 (pt request) and 1/15 patients respectively, with no major differences between the cohorts apparent. Progressive disease developed in 4/15 pts. Prolonged S.C. administration of rIL-2 is possible, in an adjuvant setting, and early discontinuation because of pt intolerance or toxicity does not appear excessive. It remains unclear which regimen is optimal in terms of patient compliance/tolerance. Adjuvant trials comparing rIL-2 to surgery alone in high risk renal cell carcinoma patients should be performed (supported by Chiron Therapeutics).

1306

BLADDER PRESERVATION IN LOCALLY ADVANCED (T2–T4) TRANSITIONAL BLADDER CARCINOMA (TBC) AFTER TRANSURETHRAL RESECTION (TUR) AND NEOADJUVANT CHEMORADIOTHERAPY. *R. Passalacqua, N. Naldi, F. Leonardi, G. Ceci, V. Franciosi, L. Bidin, V. Paietta, B. Monica, A. Prati, D. Potenzoni, G. Sanfilippo, M. Fumagalli, R. Martinelli, R. Camisa, G. Cocconi. Medical Oncology, Urology Division and Radiotherapy, Azienda Ospedaliera, Urology Division, Azienda USL, Parma, Italy.*

This is a single institution study aiming to evaluate, in muscle invasive BC, an approach of TUR, chemotherapy and pelvic radiotherapy (RT) in terms of bladder preservation, survival and toxicity. Since March 1994, 55 T2–T4 N0–N1, M0 patients (pts) entered the study. Median age was 65 (42–77); T2–T3a: 36%; T3b: 49%, T4: 13%, G3: 89%, M/F ratio: 49/6, PS 100-90: 76%, 80-60: 24%. All pts underwent an initial TUR and were treated with cisplatin (P) 20 mg/m² and 5-Fluorouracil (F) 200 mg/m² daily for 5 days on weeks 1,4 and 7. Pelvic RT (2 Gy/die for 5 days each week) was delivered on weeks 2–3 and 5–6 for a total of 40 Gy in 4 weeks. Pts were then evaluated with cystoscopy, multiple biopsies, CT scan and urine cytology. Pts with residual disease were considered as incomplete responders (IR) and an immediate cystectomy was proposed. Complete responders (CR) were treated with 2 additional PF cycles plus a further bladder RT boost with 24–28 Gy. At present 53 pts are evaluable for response; 38 (72%) achieved a complete histological response (89% for T2–T3a, 74% for T3b, 14% for T4). 15 were IR and 12 accepted an immediate cystectomy. With a median follow-up of 15 months (2–44), 5/15 (33%) in the IR group relapsed and died for distant metastasis; in the RC group 9/38 (24%) relapsed (6 in the bladder and 3 in distant sites) and 2/38 (5%) died. Toxicity was mild: neutropenia gr. 3–4: 23%; diarrhea gr. 2–3: 27%, cystitis gr. 3: 4%. Conclusions: this combined approach of TUR and alternated chemoradiotherapy induces an high rate of CR, is well tolerated even in the elderly pts, and represents a valid treatment for locally advanced TBC in a therapeutical conservative perspective.

1307

A PHASE II STUDY OF THE MULTI-TARGETED ANTIFOLATE, MTA (LY231514), IN PATIENTS WITH ADVANCED TRANSITIONAL CELL CARCINOMA (TCC) OF THE BLADDER. *L. Paz-Ares, J. Tabernero, A. Moyano, J. Rifa, H. Gomez, E. Marcuello, A. Gonzalez, I. Tarazona, H. Cortés-Funes, H. Doce de Octubre, Madrid, Spain; H. Sant Pau, Barcelona, Spain; H. R y Cajal Madrid, Spain; H. Son Dureta, Palma de Mallorca, Spain; Lilly Spain.*

MTA is a novel multi-targeted antifolate that inhibits multiple folate-dependent enzymes, including thymidylate synthase (TS), dihydrofolate reductase (DHFR) and glycinamide ribonucleotide formyltransferase (GARFT). MTA has activity in preclinical models and human tumors (breast, colon and lung). We undertook a phase II trial of MTA in 22 patients (pts) with advanced TCC of the bladder. MTA was administered as 10 minute infusions every 3 weeks, at a dose of 600 mg/m² (first 6 pts) or 500 mg/m² (subsequent pts). 18 pts are currently evaluable. 1 was ineligible (prior chemotherapy), 3 are too early. Median age was 66 years (range: 48–76); 17 were male; PS was 0 (6 pts), 1 (10 pts) and 2 (2 pts). All ts had metastatic disease; median number of disease sites: 2 (range: 1–4). 60 courses were administered, median cycles/pt: 3 (range 1–12). Five courses (8%) were dose-reduced and 6 (10%) delayed. The main toxicity was hematologic: 8 pts (44%) had grade (G) 3 and 5 pts (28%) G4 neutropenia; 4 pts developed neutropenic fever; 1 pt had G3 thrombocytopenia; 3 pts G2-4 anemia. Non-hematologic toxicity included: skin rash (G1/2: 10 pts, G3: 1 pt) preventable with dexamethasone, nausea/vomiting (G1/2: 10 pts), stomatitis (G1/2: 7 pts, G3: 1 pt), diarrhea (G3: 2 pts), and alopecia (G1: 3 pts). There were 2 toxic deaths (septicemia and renal failure). Doses were subsequently reduced to 500 mg/m² due to toxicity. Six pts (33%, 95% CI: 13–59%) had a partial remission, 4 (22%) had stable disease, 7 (39%) had progressive disease (1 pt died after the first course—reported above as the toxic death due to septicemia). Responses lasted for 1.5+ to 8 months. In conclusion, MTA has definitive antitumor activity in advanced TCC of the bladder, but its toxicity is significant.

1308

A PHASE II TRIAL OF LIPOSOMAL DOXORBICIN (DOXIL®) IN THE TREATMENT OF ADVANCED RENAL CELL CANCER: A HOOSIER ONCOLOGY GROUP (HOG) STUDY. *K. Pennington, M. Gordon, J. Picus. Hoosier Oncology Group and the Walther Cancer Institute, Indianapolis, IN.*

Metastatic renal cell cancer has few effective therapies. Standard chemotherapy has poor response rates and minimal impact on survival. Early responses in phase I trials of Doxil® in patients with advanced renal cell cancer prompted the HOG to conduct a formal phase II trial. Between 7/10/96 and 11/7/97 a total of 32 patients was entered onto this trial. Eligibility criteria included biopsy proven renal cell cancer that was metastatic or unresectable, KPS > 60%, no prior chemotherapy, ≤1 prior immunotherapy regimen, Creatinine ≤2.5, and no clinical evidence of compromised cardiac function. Patients received 50 mg/m² IV every 28 days. Standard dose reductions for cytopenia were employed, along with dose reductions for plantar-palmar erythema. The patients ranged in age from 38–78 years (median 60) with a median KPS of 90. Twelve patients had previous immunotherapy. A maximum of eight cycles was allowed, and five patients received that number of cycles. The median number of cycles was three. One patient showed a partial response based on standard criteria, which lasted 190 days. Thirteen additional patients showed stable disease, that lasted a median of 105 days. Fourteen patients showed progressive disease, without evidence of disease stabilization. The median survival is 10 months, with 19 patients still alive. Major grade III or IV toxicities included fatigue (4), leukopenia (3), skin or hand-foot syndrome (3), stomatitis or mucositis (2), constipation (2), infection (1), nausea or vomiting (1). More minor nausea (grade I or II) was seen in 6 other patients. Only 2 patients had grade I and 1 patient had grade II cardiotoxicity. This regimen was very well tolerated, but unfortunately only exhibited minimal evidence of tumor response.

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