Cisplatin, Gemcitabine, and Paclitaxel Triplet Chemotherapy in 50 Patients With Locally Advanced or Metastatic Urothelial Cancer

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Background A pilot phase 2 study at West Virginia University investigated cisplatin, gemcitabine, and paclitaxel "triplet" chemotherapy for urothelial cancer.

Methods Cisplatin (50 mg/m^2), gemcitabine (1,000 mg/m^2), and paclitaxel (75 mg/m^2) were given days 1 and 8 of a 3- to 4-week cycle to 50 patients (35 men; 15 women) with a median age of 68 years (range, 41-82 years).

Results Histologic tests identified transitional cell carcinoma alone in 38 patients (76%) or with adenocarcinoma or squamous carcinoma in 12 patients (24%). Thirty-one M0 patients (62%) had advanced regional disease, and 19 M1 patients (38%) had metastases. At treatment, the NCI performance status was 2 in 11 patients (22%) and 3 to 4 in 17 patients (34%). Two hundred and eighteen chemotherapy cycles were administered. Grade 3 or 4 toxicity occurred in 33% of patients. Objective tumor responses occurred in 17 M0 patients (55%) and in 11 M1 patients (58%). Complete responses occurred in 11 M0 patients (35%) and 2 M1 patients (11%). Median survival for M0 patients, M1 patients, and all 50 patients was 16.8, 13.5, and 14.1 months, respectively.

Conclusions Triplet chemotherapy is active in advanced urothelial cancer with manageable toxicity. More proactive ancillary support might improve these results. Stringent protocol eligibility criteria (eg, E-5899) excluded 70% of our patients from a standard clinical trial. Less stringent eligibility criteria might allow more rapid accrual to national trials.

Condensed Abstract

A phase 2 study combining cisplatin, gemcitabine, and paclitaxel in 50 patients with advanced local or metastatic urothelial cancer found a 56% overall and 26% complete response rate, with 14.1-month median survival. Seventy percent of these patients did not meet standard clinical trial eligibility (eg, E-5899), and 34% were National Cancer Institute performance status 3 or 4.

Introduction

In 2004, there were 60,000 new diagnoses of bladder cancer and more than 12,000 deaths from bladder cancer in the United States.[1] The combination of methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC)[2] and the 3-drug combination of cisplatin, methotrexate, and vinblastine without doxorubicin[3] have both significantly improved the treatment of metastatic bladder cancer. In a phase 3 intergroup trial, MVAC was found to be more toxic than single-agent cisplatin but to have a superior response rate (39% vs 12%) and significantly greater progression-free (10 mo vs 4.3 mo) and overall (12.5 mo vs 8.2 mo) survival.[4]

Randomized studies demonstrate improved survival of patients with metastatic urothelial cancer after treatment with MVAC. However, after 5 or more years of follow-up, only 3% of patients with advanced disease who received MVAC were still alive and free of disease.[5]

Recent studies suggest that response rates and survival comparable to those found with MVAC can be achieved with cisplatin in combination with either or both paclitaxel or gemcitabine.[6] These newer combinations also seem less toxic than MVAC.

On the basis of a phase 1 to 2 dose-finding study of cisplatin, gemcitabine, and paclitaxel (CGP) therapy in advanced non–small cell lung cancer patients,[7,8] we initiated a phase 2 cohort study. We assessed the safety and efficacy of CGP in patients with urothelial cancer who had declined primary surgery or radiotherapy, who were considered a poor surgical risk by referring urologists, or who had disease relapse or progression after initial standard therapy.

The primary goals of this study were to establish: 1) a clinical profile of patients with advanced urothelial cancer who were referred to us at West Virginia University, including how many of our patients met standard eligibility criteria for NCI-sponsored clinical trials (eg, E-5899); 2) CGP toxicity; 3) CGP tumor response rates, and 4) patient survival posttreatment. The study was approved by the institutional review board.

Methods

Fifty patients 18 years of age or older gave informed consent for treatment with CGP. All 50 patients had biopsy-proven urothelial cancer, including transitional cell carcinoma, adenocarcinoma, squamous cell carcinoma, or cancer with mixed histologic findings. Patients had high-grade muscle invasive disease (T2, G3), locally advanced disease (T3, T4, or N1-N3), or metastatic disease (M1).

Patients who had prior malignancy were allowed to participate if they had been treated with curative intent and if the malignancy was judged to be clinically inactive. Those who had prior surgery, radiotherapy, immunotherapy, or chemotherapy were treated if 4 or more weeks had elapsed since their last treatment.

Patients were analyzed by metastatic status: M0 patients received as many as 4 cycles of CGP chemotherapy for locally advanced disease before they were reevaluated for possible surgery or radiotherapy; M1 patients received continuous CGP chemotherapy for systemic disease until disease progression, dose-limiting toxicity, or death.

Before treatment, patients provided a thorough history and had a physical examination. During chemotherapy, complete blood cell, platelet, and differential blood counts were repeated every 1 to 2 weeks, and a chemistry panel (measuring electrolytes, blood urea nitrogen, creatinine, and liver function) was repeated monthly.

Patients were generally seen monthly during chemotherapy; after chemotherapy, they were seen at intervals of 3 to 4 months. At each visit, patients provided an interval history and had a physical examination with appropriate laboratory and imaging tests.

Patients received dexamethasone 20 mg by mouth the night before chemotherapy and 10 to 20 mg intravenously immediately before chemotherapy. Before chemotherapy, patients received cimetidine 300 mg intravenously, diphenhydramine 50 mg intravenously, and granisetron 2 mg by mouth or 10 μg/kg intravenously and 1,000 mL normal saline with 20 to 40 mEq KCl and 1 to 2 g $MgSO_4$ intravenously at 350 mL/hr.

CGP chemotherapy dosing was planned per Frasci and colleagues,[7,8] who administered cisplatin 50 mg/m^2, gemcitabine 1,000 mg/m^2, and paclitaxel 75 mg/m^2 intravenously, using actual body weight on days 1 and 8 of a 21-day cycle. Gemcitabine was administered first, followed by paclitaxel, then cisplatin; each medication was administered separately in 250 mL normal saline for 30 to 60 minutes.

After chemotherapy, the patients received 500 mL normal saline with KCl and $MgSO_4$. When needed for diuresis, furosemide (5-10 mg) was given intravenously. Chemotherapy doses were adjusted, with each cycle based on the patient's clinical evaluation and previous toxicity. Doses were reduced 25% or cycles were delayed when nadir neutrophil counts fell below 1.5×10^9 cells/L or nadir platelet counts fell below 75×10^9/L. Cytokine support, transfusions, and antibiotics were used if a specific toxicity developed that required treatment.

Toxicity to medications was assessed using the common toxicity criteria of the National Cancer Institute 1998.[9] Treatment-related death was scored for any death occurring within 1 month of chemotherapy. Any patient who received any portion of a treatment cycle was considered eligible for evaluation of toxicity, tumor response, survival, and outcome.

The objectively measurable tumor response was assessed using standard 2-dimensional criteria. Survival was defined as the time from the first cycle of chemotherapy to death or last follow-up. Survival curves were calculated using the Kaplan-Meier method[10] and JMP statistical software (version 4; SAS Institute, Inc, Cary, North Carolina). Statistical differences between patient subsets were calculated using the log-rank test. Body surface area, ideal body weight, and calculated creatinine clearance were determined using dosing tools from MICROMEDEX (vol 118; Thomson, Greenwood Village, Colorado).

Results

Fifty patients (31 M0; 19 M1) with urothelial cancer received CGP chemotherapy. The "on study" parameters are listed in Table 1. The 31 M0 patients had regional disease confined to the pelvis or upper urinary tract, whereas the 19 M1 patients had metastases as defined by the tumor-node-metastasis (TNM) classification system of the American Joint Committee on Cancer (1997).[12]

Before starting CGP chemotherapy, 2 patients had a nephrectomy for primary urothelial cancer of the upper tract. Seven of the M0 patients (23%) and 9 of the M1 patients (47%) had undergone a prior exploratory laparotomy in which the tumor was judged nonresectable. Twenty-two patients overall (44%) had obstructive uropathy that required ureteral stenting (internal, external, or both). Previously, 25 (50%) of the 50 patients had received intravesical bacille Calmette-Guérin (BCG), and 12 (24%) of the 50 patients had received intravesical chemotherapy.

Four (21%) of the 19 patients treated for M1 disease had previously received systemic chemotherapy: 1) A 58-year-old woman received 4 cycles of adjuvant MVAC, 2 before and 2 after cystectomy. About 2 years later, she had ilial conduit and nodal relapse. With CGP chemotherapy, lymph nodes responded but progressive squamous cell cancer occurred in the ilial pouch. 2) An 82-year-old man had postcystectomy CGP as an adjuvant therapy, but had a biopsy-proven relapse in bone a year later. He then had a clinical complete response to palliative CGP and lived 2 years longer. 3) A 56-year-old woman had extensive pelvic disease that initially responded to 3 cycles of cisplatin and paclitaxel, but disease relapsed 16 months later and did not

respond to subsequent cycles of CGP. 4) A 52-year-old man with extensive metastatic disease involving nodes and skin had prior therapy with 4 cycles of MVAC, 5 cycles of carboplatin and taxol, and 3 cycles of MVA with carboplatin. He did not respond to a brief trial of CGP chemotherapy.

Comorbid conditions of study participants are listed in Table 2. Most notably, 40 patients (80%) had a history of active smoking, with an average of 50 pack-years. Four other patients (8%) reported heavy exposure to passive smoking in their home or work environment. Furthermore, these 50 patients reported having 6 first-degree relatives with bladder cancer and 9 with lung cancer. Other frequently reported comorbid conditions included hypertension (56%), emphysema (44%), coronary artery disease (38%), peripheral vascular disease (22%), creatinine clearance less than 50 mL/min (24%), and diabetes mellitus (20%).

The first 4 CGP chemotherapy treatment cycles and the percentage of the planned target dose[7,8] administered during the first 4 cycles are summarized in Table 3. The M0 patients received approximately 85% of the planned dose both day 1 and day 8, with 105 day 1 doses followed by 76 (72%) day 8 doses. Similarly, M1 patients received approximately 80% of the planned doses on both day 1 and day 8, with 64 day 1 doses followed by 48 (75%) day 8 doses.

NCI grade 3 or 4 toxicity was assessed in all 50 patients (Table 4). A total of 218 cycles were administered. Three patients (6%) died within 1 month after chemotherapy and were scored as “toxic deaths.” However, 1 of these deaths occurred after a sixth cycle during clinical disease progression and thus may not have been related to the chemotherapy. The most common NCI grade 3 or 4 toxicity was hematologic, with about one-third of the patients and about 10% of the cycles associated with neutropenia, thrombocytopenia, or severe anemia requiring transfusion.

Objectively measurable tumor responses to CGP chemotherapy are listed in Table 5. Objective responses occurred in 17 (55%) of 31 M0 patients, in 11 (58%) of 19 M1 patients, and in 28 (56%) of all 50 patients. Complete response was observed in 11 (35%) of 31 M0 patients, in 2 (11%) of 19 M1 patients, and in 13 (26%) of all 50 patients. Tumor response to CGP chemotherapy was not significantly related to performance status (0-2 vs 3-4), body mass index (<28 vs >28), presence of histologic findings of adenocarcinoma or squamous cell cancer, or status of disease as locally advanced (M0) or metastatic (M1) (data not shown).

Median survival from the start of CGP chemotherapy (Table 6) appeared to be significantly related to tumor response (Fig. 1), ECOG performance status (0-2 vs 3-4),

eligibility for clinical trial E-5899, and presence or absence of an internal or external stent at the onset of treatment. However, survival after CGP chemotherapy did not appear significantly related to age, sex, advanced regional (M0) vs metastatic (M1) disease, body mass index, presence of histologic findings of adenocarcinoma or squamous cell cancer, or prior laparotomy, cystectomy, or intravesical bacille Calmette-Guérin immunotherapy.

The median survival (Fig. 2) was 16.8 months for M0 patients, 13.5 months for M1 patients, and 14.1 months for all 50 patients (confidence interval, 8.7-17.7 months). The survival of these patients was compared with that of patients with similar-risk urothelial cancer treated with MVAC chemotherapy at Memorial Sloan-Kettering Cancer Center.[11] We assigned risk factors used at Memorial Sloan-Kettering to our group of 50 patients and calculated that a risk-adjusted median survival would have been 15.4 months (confidence interval, 11.5-24 months) for MVAC-treated patients with similar risk.

Discussion

De Wit and Bellmunt[13] have thoroughly reviewed the evolution of chemotherapy for patients with advanced urothelial cancer, including the more recent use of taxanes and gemcitabine.

In 1985, researchers at Memorial Sloan-Kettering reported an overall response rate of 71% in 24 patients to the 4-drug MVAC regimen.[2] This was later updated to an overall response rate of 72% in 121 patients, with a clinical complete response of 18% and a pathologic complete response of 11% with postchemotherapy surgery.[14] Other authors later confirmed an overall response rate to MVAC of 40% to 57%, with a complete response rate of 13% to 19%[15-17] and a median survival of 12 to 13 months.

MVAC is associated with significant morbidity in the typical elderly patient who has metastatic urothelial cancer and tobacco-related pulmonary or cardiovascular disease or impaired renal function. Even in patients in good clinical condition, MVAC is associated during therapy with as much as a 25% incidence of granulocytopenic fever, a 50% grade 2 to 3 mucositis, and a 3% drug-related mortality.[2,4,14-19]

In MVAC-treated patients, impaired performance status, weight loss, high alkaline phosphatase, and metastases to liver, lungs, or bones were adversely related to a response to chemotherapy.[4,20] The 2 most important independent prognostic factors affecting median survival were performance status and visceral metastases.[11] Median survival for patients with 0,

1, or 2 risk factors was 33, 13.4, and 9.3 months, respectively (P<.001). Overall, 3.7% of MVAC-treated patients survived disease free for more than 6 years.[5,19]

From 1994 to 2000, substantial single-agent activity in urothelial cancer was found for the taxanes paclitaxel and docetaxel and for gemcitabine.[21-31]

In previously untreated patients, phase 2 responses to paclitaxel or docetaxel were 25% to 40% vs 17% for single-agent cisplatin.[23,31] Unfortunately, these new taxanes appeared less effective for patients who had been treated previously with cisplatin-based chemotherapy.[25,28,29] Phase 2 studies of 2-drug combinations of cisplatin and docetaxel or cisplatin and paclitaxel found response rates in untreated patients similar to those treated with MVAC.[32-37]

Gemcitabine tested in phase 1 and phase 2 studies in patients with locally advanced and metastatic urothelial cancer[21,22,24,26,27,30] had an overall response rate of 27% that did not appear to be influenced by previous cisplatin-based chemotherapy, which suggests incomplete cross-resistance between these agents. Furthermore, cisplatin and gemcitabine were synergistic,[38,39] and the toxicity profile of gemcitabine was favorable. The 2-drug combination of cisplatin and gemcitabine (CG) had a response rate of 41% to 57%, and a median survival of 14.3 to 13.2 months, which was similar to that of MVAC.[40-43]

In 1999, Bajorin and colleagues[11] at Memorial Sloan-Kettering identified independent prognostic factors in 203 patients who had unresectable or metastatic transitional cell carcinoma. By multivariate analysis, 2 factors had independent prognostic significance: Karnofsky performance status of less than 80% (NCI performance status >1) and visceral metastases. Of note, the median survival of the patient cohorts at Memorial Sloan-Kettering was 9 to 26 months, depending on the proportion of patients with different risk factors. When these risk factors were assigned to our 50 patients, the expected median survival of MVAC-treated patients at Memorial Sloan-Kettering who had risk factors similar to those of our CGP-treated patients was 15.4 months (confidence interval, 11.5-24 mo).[11] Thus, the observed median survival of 14.1 months for our patients (confidence interval, 8.7-18.7 mo) is similar to that of the MVAC-treated patients at Memorial Sloan-Kettering.

In 2000, von der Maase et al[6] reported a large multinational phase 3 trial comparing CG with MVAC. Overall survival for CG was similar to that for MVAC (13.8 vs 14.8 months), as were time to progression (7.4 months for both arms of the study) and overall response (49% vs 46%). Fewer patients on CG vs MVAC had grade 3 or 4 neutropenia (71% vs 82%), neutropenic

fever (2% vs 14%), neutropenic sepsis (1% vs 12%), grade 3 or 4 mucositis (1% vs 22%), or toxic death (1% vs 3%). More patients on CG than on MVAC had grade 3 or 4 anemia and thrombocytopenia. Thus, CG was established as a valuable therapeutic alternative to MVAC for patients who had metastatic bladder cancer.

Also in 2000, Bellmunt and colleagues[44] published phase 1 and phase 2 trials of the triplet combination of CGP in 61 patients. Together, the phase 1 study (15 patients) and the phase 2 study (46 patients) had an overall response rate of 78% and a median survival time of 24 and 16 months, respectively. In our patients with advanced urothelial cancer and a poor prognosis, CGP was an active triplet regimen with a tumor response of 56% overall and 26% complete response.

CGP chemotherapy provided significant palliation for a 73-year-old patient with stage IV pelvic transitional cell carcinoma invading the rectum; he had a complete, biopsy-confirmed remission lasting longer than 50 months after CGP chemotherapy alone (he declined subsequent surgery or radiotherapy). Similarly, an 82-year-old patient with biopsy-proven painful bone metastases had a clinical complete remission during CGP chemotherapy lasting 15 months before a solitary brain stem relapse developed. After radiotherapy of the central nervous system, he lived 12 months longer.

As documented in our patients, CGP had moderate toxicity. However, at the time of this study, blood transfusions, cytokines, and antibiotics were used conservatively, usually after toxicity developed. The original MVAC trials were conducted without cytokine support and with rare use of blood transfusions. More proactive ancillary support during CGP or MVAC therapy might decrease toxicity and improve results.

Of note, eligibility for participation in clinical trials was limited in our patients. For example, E-5899 was a contemporary study of gemcitabine and taxol chemotherapy for advanced urothelial cancer. Applying E-5899 criteria to our patients, 35 (70%) of the 50 patients did not meet protocol eligibility criteria. The CGP patients who did meet E-5899 eligibility criteria had a significantly better survival than did the noneligible patients (median survival, 22.4 months vs 8.8 months; P=.001).

Overall, we consider our patient survival to be unsatisfactory. Further improvement in systemic therapy for advanced urothelial cancer is needed.

Along with other groups, the EORTC (European Organization for Research and Treatment of Cancer) has initiated a randomized phase 3 study of CGP triplet vs CG doublet

therapy; 610 patients (performance status, 0 or 1; creatinine clearance, >1 mL/s) will be required to detect a survival improvement of 4 months (from 14 to 18 months). Perhaps liberalizing eligibility criteria would allow more rapid accrual with more rapid therapeutic progress.[45]

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Legends

Fig. 1. Months of patient survival vs tumor response. Top line is complete response (*N*=13); middle line is partial response (*N*=15); and bottom line is no response (*N*=22) (*P*<.001).

Fig. 2. Months of patient survival for locally advanced (M0) versus metastatic (M1) disease. Top line is M0 (*N*=31); bottom line is M1 (*N*=19) (*P*=NS).

Table 1. Profile of 50 Patients With Locally Advanced (M0) or Metastatic (M1) Urothelial Cancer Treated With Cisplatin, Gemcitabine, and Paclitaxel

Characteristic	M0	M1	Total, no. (%) M0+M1
No. of patients	31	19	50
Age, y			
Median	69	66	68
Range	41-81	45-82	41-82
Sex			
Male	20	15	35
Female	11	4	15
Prior treatment, no. of patients			
TURB or partial cystectomy	30	18	48
Laparotomy (exploratory only)	7	9	16
Stent, external	12	2	14
Stent, internal	5	5	10
Cystectomy	0	6	6
Nephrectomy (upper tract, primary)	1	1	2
Immunotherapy, intravesical BCG	12	13	25
Chemotherapy, intravesical	7	5	12
Chemotherapy, systemic	0	4*	4
Radiotherapy	1†	2	3

Table 1 (continued)

Characteristic	M0	M1	Total, no. (%) M0+M1
NCI performance status			
PS0	2	0	2 (4)
PS1	15	5	20 (40)
PS2	6	5	11 (22)
PS3	6	9	15 (30)
PS4	2	0	2 (4)
MSKCC adverse risk factors[11]			
0 (low risk)	16	5	21 (42)
1 (intermediate risk)	15	2	17 (34)
2 (high risk)	0	12	12 (24)
Histologic findings			
Transitional cell cancer only	22	16	38
Transitional cell cancer mixed	6	2	8
Squamous cell cancer only	3	1	4
Adenocarcinoma only	0	0	0
Grade			
High (3)	28	13	41
Low (1,2)	3	3	6
Unspecified	0	3	3

Table 1 (continued)

Characteristic	M0	M1	Total, no. (%) M0+M1
TNM stage[12]			
S2	9	-	9
S3	9	-	9
S4	13	19	32
Active disease sites			
Bladder	30	13	44
Nodes (regional)	8	7	15
Bones	0	8	8
Lungs	0	6	6
Nodes (extrapelvic)	0	6	6
Liver	0	4	4
Other	0	4	4
Skin	0	1	1
Central nervous sytem or adrenal	0	0	0
Total no. disease sites per patient			
1	23	2	25
2	8	7	15
3+	0	10	10

Table 1 (continued)

AJCC, American Joint Committee on Cancer; BCG, bacille Calmette-Guérin; MSKCC, Memorial Sloan-Kettering Cancer Center; NCI, National Cancer Institute; TNM, tumor-node–metastasis; TURB, transurethral tumor resection.

*These 4 patients had received various prior chemotherapies before receiving cisplatin, gemcitabine, and paclitaxel.

†Prior radiotherapy for prostate cancer.

Table 2. Comorbid Conditions in Patients With Urothelial Cancer Treated With Cisplatin, Gemcitabine, and Paclitaxel*

Condition	No.	%
Smoking		
Active	40	80
Heavy passive	4	8
Weight loss (*N*=41)		
>5%	27	66
>10%	10	24
Hypertension	28	56
Nephrostomy or stents	22	44
Anemia	22	44
Emphysema	22	44
Coronary artery disease		
Active or prior	19	38
Obesity or overweight, BMI >28 (*N*=49)	18	37
Creatinine clearance <50 mL/min (<0.83 mL/s) (*N*=49)	12	24
Peripheral vascular disease	11	22
Diabetes mellitus	10	20
Deep venous thrombosis, prior history	5	10

Table 2 (continued)

Condition	No.	%
Malignancy, prior history	1	2

BMI, body mass index.

*N=50 unless otherwise indicated.

(MAC)

Table 3. Actual Cisplatin, Gemcitabine, and Paclitaxel Dose as a Percentage of the Planned Chemotherapy Dose During the First 4 Cycles

Cycle (d)	No. of patients	Percentage of planned dose, mean		
		Cisplatin	Gemcitabine	Paclitaxel
M0 patients (*N*=31)				
1 (1)	31	80	82	81
1 (8)	25	81	83	85
2 (1)	27	80	83	84
2 (8)	16	83	84	86
3 (1)	24	82	85	86
3 (8)	19	83	79	85
4 (1)	23	81	82	85
4 (8)	16	82	85	85
M1 patients (*N*=19)				
1 (1)	19	77	79	79
1 (8)	15	76	80	80
2 (1)	16	76	80	80
2 (8)	12	71	77	77
3 (1)	16	78	81	81
3 (8)	11	75	80	80
4 (1)	13	81	83	85
4 (8)	10	81	86	86

(MAC)

Table 4. NCI Grade 3 or 4 Toxicity in 50 Patients With Advanced Urothelial Cancer Treated With 218 Cycles of Cisplatin, Gemcitabine, and Paclitaxel

	Patients		Cycles	
Findings of toxicity	No.	%	No.	%
Hematology				
ANC $<1\times10^9$/L	18	36	24	11
Platelets $<50\times10^9$/L	17	34	25	12
Hgb <8 mg/dL or RBC transfusion	14	28	24	11
Infection (any ANC)	14	28	18	8.3
Gastrointestinal (enteritis, dehydration, LFT, etc)	11	22	12	6.7
Neurologic (sensory-motor, seizure, etc)	5	10	5	2.3
Urologic (creatinine >3×ULN, dialysis)	4	8	4	1.8
Death <1 month postchemotherapy	3*	6	3	NA

ANC, absolute neutrophil count; LFT, liver function tests; NA, not applicable; RBC, red blood cells; ULN, upper level of normal.

*A 65-year-old man with widespread metastases died on day 3 of cycle 1; a 76-year-old man with extensive cancer and comorbidity died on day 6 of cycle 1; and a 77-year-old man with disease progression and deep vein thrombosis died during cycle 6.

(MAC)

Table 5. Objective Tumor Responses After Treatment With Cisplatin, Gemcitabine, and Paclitaxel

Response type	M0 (*N*=31)		M1 (*N*=19)		M0+M1 (*N*=50)	
	No.	%	No.	%	No.	%
Complete (clinical, pathologic)	5,6	35	1,1	11	13	26
Partial	6	19	9	47	15	30
Total	17	55	11	58	28	56
None	14	45	8	42	22	44

Table 6. Survival of Patient Subsets After Cisplatin, Gemcitabine, and Paclitaxel Chemotherapy

Description*		No. of patients	Median survival, mo	*P* value
Tumor response to CGP	Complete	13	23.2	<.001
	Partial	15	12.2	
	None	22	5.6	
NCI performance status	0-2	33	18.7	.001
	3-4	17	8.2	
ECOG 5899 study eligible	Yes	15	22.4	.001
	No	35	8.8	
Prior internal or external ureteral stent	Yes	22	8.1	.03
	No	28	18.7	
MSKCC risk factors	WVU-CGP	50	14.1 (CI, 8.7-18.7)	Observed
Bajorin et al 1999[11]	MSKCC-MVAC	203	15.4 (CI, 11.5-24.0)	Calculated

CGP, cisplatin, gemcitabine, paclitaxel; ECOG, Eastern Cooperative Oncology Group; MSKCC, Memorial Sloan-Kettering Cancer Center; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; NCI, National Cancer Institute; WVU, West Virginia University.