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A phase 1/1b study of satraplatin (JM-216) in combination with docetaxel in patients with advanced solid tumors and metastatic castrate-resistant prostate cancer★

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Abstract

Background—Satraplatin is an oral platinum with potential advantages over other platinum agents. This study investigated the combination of satraplatin and docetaxel in a phase 1 study of patients with advanced solid tumor malignancies followed by a phase 1b study in men with chemotherapy naïve metastatic castrate-resistant prostate cancer (CRPC).

Methods—In this single institution phase 1/1b study, patients received docetaxel on day 1 and satraplatin on days 1–5 of a 21-day cycle $\pm$ granulocyte colony stimulating factor (G-CSF). For phase 1b, prednisone 10 mg daily was added.

Results—Twenty-nine patients received treatment. Based on 3 dose limiting toxicities (DLT) (grade 4 neutropenia) in 13 patients at dose levels 1 and –1 (docetaxel 60 mg/m² plus satraplatin 40 mg/m² and docetaxel 60 mg/m² plus satraplatin 50 mg/m²) G-CSF was administered with subsequent cohorts. A dose level of docetaxel 60 mg/m² plus satraplatin 50 mg/m² with G-CSF was the starting dose level for phase 1b. At the highest dose in the phase 1b (docetaxel 75 mg/m² plus satraplatin 50 mg/m²) there were no DLTs.

Conclusion—The combination of satraplatin and docetaxel is feasible in solid tumor malignancies. In advanced malignancies, the recommended phase 2 dose is docetaxel 60 mg/m² IV day 1 with satraplatin 40 mg/m²/d PO days 1–5, without G-CSF, and Docetaxel 70 mg/m² IV day 1 with Satraplatin 50 mg/m²/day PO days 1–5, with G-CSF support, repeated in 3-week cycles. For patients with CRPC the recommended phase 2 dose is docetaxel 75 mg/m² IV day 1 with satraplatin 50 mg/m²/d PO days 1–5, with G-CSF and prednisone 10 mg daily, repeated in 3-week cycles.

Keywords

Satraplatin; Docetaxel; Phase 1; Castrate-resistant; Prostate; Cancer

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1. Introduction

Platinum agents have proven efficacy against a wide range of solid tumors. Currently, 3 platinum agents are approved by the Food and Drug Administration (FDA) for clinical use; cisplatin, carboplatin, and oxaliplatin. Despite their efficacy, these platinum-based agents are associated with significant toxicity including neurotoxicity, nephrotoxicity, myelosuppression, and ototoxicity, and require intravenous administration. Satraplatin (JM 216) is an orally administered fourth generation platinum analogue designed to optimize the therapeutic efficacy of platinum, while limiting toxicity [1]. Like the other platinum, it intercalates into DNA leading to cell cycle arrest in the G₂ phase [2].

Aside from its oral administration, another potential advantage for satraplatin is its potential to overcome platinum resistance [3–5]. After phase 1 testing using single agent satraplatin the optimal dosing administration ranged from 100 to 120 mg/m² daily for 5 days repeated every 21 or 28 days [6–9]. In these trials, there was no neurotoxicity, ototoxicity, or nephrotoxicity. The dose-limiting toxicities were thrombocytopenia and neutropenia, which were reversible and non-cumulative. The most common grade 3 to 4 toxicities were gastrointestinal, including nausea, vomiting, and diarrhea, each occurring in 10% of the patients.

In vitro studies have demonstrated that satraplatin has antineoplastic activity against several cells lines including prostate [10]. Clinical testing with satraplatin has demonstrated activity for the treatment of several solid tumors, including CRPC [11–15]. Currently, docetaxel is FDA approved and is the standard of care for the treatment of metastatic CRPC based on its survival benefit [16,17]. In vitro, the combination of docetaxel and satraplatin was shown to have synergistic effects, thus providing a rationale for this trial [18].

To determine the tolerability and feasibility of satraplatin plus docetaxel, we conducted a phase 1 dose escalation trial in patients with advanced solid tumor malignancies with a planned phase 1b expansion in chemotherapy naïve men with metastatic CRPC.

The primary objective of phase 1 was to define the maximum tolerated dose of satraplatin in combination with docetaxel. The primary objective of phase 1b was to determine a recommended phase 2 dose with the addition of prednisone in men with chemotherapy naïve metastatic CRPC.

2. Patients and methods

2.1. Patient selection

This was a single institution, single arm, open label phase 1 dose escalation study with a phase 1b component in men with CRPC. All patients were over 18 years of age with an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2 and at least a 3-month life expectancy. The protocol was approved by the institutional review board at the University of Wisconsin and all patients provided written informed consent. Patients in phase 1 had a histologically confirmed solid malignancy that was refractory to standard therapy or for which no curative standard therapy was available. Other inclusion criteria included: measurable or evaluable disease, and adequate organ function defined as absolute neutrophil count (ANC) 1,500/mm³, platelet count 100,000/mm³, total bilirubin upper limit of normal (ULN), and serum creatinine 1.7 mg/dl and creatinine clearance > 50 ml/min, using the Cockcroft Gault equation. A serum aspartate aminotransferase and alanine aminotransferase of <5× ULN was permitted provided they were associated with a predefined level of alkaline phosphatase.

Exclusion criteria for phase 1 included prior treatment with docetaxel or a platinum agent <3 months from the time of enrollment or <4 weeks since any other prior chemotherapy. Other exclusion criteria general to both the phase 1 and expansion cohort included: <4 weeks since prior radiotherapy, evidence of concurrent second malignancy, greater than grade 1 pre-existing peripheral neuropathy, edema, or ototoxicity, concurrent use of medications that inhibit cytochrome P450 3A4, untreated brain metastases, or any condition that would place the patient at excessive or unacceptable risk of toxicity.

Patients in the 1b portion of the study included men with histologically confirmed adenocarcinoma of the prostate who were surgically castrate or medically castrate with the use of hormonal therapy (estrogen therapy, luteinizing hormone receptor antagonist + casodex) and documented to have a serum testosterone <50 ng/ml. Other inclusion criteria were adequate organ function as defined above for the first cohort, along with progressive disease defined by new lesions on bone scan or new/enlarging lesions on CT scan, or metastatic disease and rising prostate specific antigen (PSA) within 4 weeks prior to registration. Treatment with flutamide must have been discontinued 4 weeks prior to registration with continued evidence of progression. For bicalutamide or nilutamide, patients must have discontinued the drug 6 weeks prior to registration with evidence of progression.

Exclusion criteria specific to this cohort of men with CRPC included: no prior cytotoxic chemotherapeutic treatment was allowed, however, up to 1 prior experimental therapy (non-cytotoxic) was permitted as long as it was given >4 weeks prior to study entry, radiation therapy performed <4 weeks prior to study as long as it involved less than 25% of the bone marrow, treatment with strontium 89, samarium 152, or other radioisotope, concurrent use of estrogen, or estrogen-like agents.

2.2. Treatment

Docetaxel was administered intravenously over 1 hour on day 1 and satraplatin orally on days 1–5 of each 21-day cycle. If granulocyte colony stimulating factor (GCSF) was administered, it was given on day 6. For phase 1, dexamethasone was given orally 8 mg twice daily for 3 days, beginning 24 hours before the docetaxel infusion. For phase 1b, dexamethasone orally 8 mg was given 12, 3, and 1 hour(s) prior to docetaxel. Satraplatin was taken orally on an empty stomach approximately 24 hours apart. The first dose was taken within 2 hours following docetaxel infusion. Patients received scheduled 5-HT₃ receptor antagonist prior to oral administration of satraplatin on days 2–5. In the dose expansion cohort, prednisone 5 mg was administered twice daily continuously throughout the study duration. The patients were continued on study until disease progression or toxicity according to predefined criteria.

2.3. Assessment

Tumor lesions were measured using response evaluation criteria in solid tumors (RECIST [19]) 1.0 at baseline and every 2 cycles. A complete response was defined as the disappearance of all known disease during 2 observations at least 4 weeks apart. For patients with bone only disease, normalization of the bone scan was required. A partial response was defined as 30% decrease in sum of the greatest perpendicular tumor diameters of all measurable disease documented for 4 weeks. Progressive disease included any unequivocal increase of 20% in the sum of the greatest perpendicular tumor diameters of all measurable disease, or the appearance of any new lesion. Stable disease was any other condition not met by the criteria outlined in complete response, partial response, or progression.

Adverse events were evaluated at the start of each 21-day cycle. They were graded using the National Cancer Institute Common Terminology Criteria (NCI CTCAE) ver. 3.0. Prostate

specific antigen (PSA) testing occurred at the start of every cycle. Laboratory parameters including complete blood counts with differential and serum chemistries were obtained weekly.

For hematologic toxicity, scheduled doses with both chemotherapeutic agents were withheld for platelets $100,000/\text{mm}^3$ or neutrophil count $1,500/\text{mm}^3$. If platelet count was $<50,000/\text{mm}^3$, there was a $10 \text{ mg}/\text{m}^2$ dose reduction in satraplatin and 25% dose reduction of docetaxel after platelets recovered to $100,000/\text{mm}^3$. If the recovery of platelets to $>100,000/\text{mm}^3$ required a delay in treatment > 2 weeks, therapy with both agents was discontinued.

If patients required >2 dose reductions of docetaxel or satraplatin and/or the dose of docetaxel was reduced to $<30 \text{ mg}/\text{m}^2$ treatment was discontinued. If the recovery of platelets to $>100,000/\text{mm}^3$ or any toxicity that requires a delay in therapy >2 weeks, therapy with both agents was discontinued.

For the phase 1 portion, by definition a DLT occurred in the first cycle and must have been considered at least possibly related to the study drugs. A DLT was reported if the following toxicity was noted: (1) grade 3/4 neutropenia, lasting for >5 days or grade 4 neutropenia associated with fever, (2) grade 3/4 thrombocytopenia lasting for >5 days, (3) or any non-hematologic >3 grade 3 toxicity as per NCI CTCAE. For nausea, vomiting, and diarrhea, grade 3 toxicity was not considered a DLT if it was controlled with maximal anti-emetics or anti-diarrheals.

For phase 1b a DLT was reported if the adverse event occurred during the first cycle and was at least possibly attributable to the combination of docetaxel and satraplatin. A DLT was reported if the following toxicity was noted: (1) grade 4 toxicity ($\text{ANC} < 500/\text{mm}^3$) for 7 days or febrile neutropenia, (2) platelet count $25,000/\text{mm}^3$ lasting 7 days or $50,000/\text{mm}^3$ with associated severe and life-threatening (or intracranial) bleeding, (3) or any non-hematologic grade 3 as per NCI CTCAE. For nausea and vomiting, grade 3 toxicity was not considered a DLT if it was not controlled with maximal anti-emetics.

Dose escalation was performed using a standard dose escalation design with 3 to 6 patients per dose level. Specifically, at least 3 patients assessable for toxicity were treated at each dose level. If none of the first 3 patients experienced a DLT, the next dose level was initiated. If a DLT occurred in 1 patient, 3 additional patients were treated at the same level. Dose escalation was only continued if DLTs were observed in no more than 1 patient of the expanded cohort. If a DLT occurred in at least 2 patients, dose escalation was stopped and subsequent patients were treated at the previous level that was defined as the MTD.

3. Results

3.1. Study population

Twenty-nine patients were registered and enrolled into the study at 2 centers within 1 institution between July 2005 and January 2009. Twenty-three participated in the phase 1 portion, and six in the 1b portion. Demographics and baseline disease characteristics for all patients are listed in Table 1.

3.2. Chemotherapy administration

The dose levels, number of patients in each dose level cohort, DLTs, and number of cycles per dose level are listed in Table 2. All patients received at least 1 cycle of treatment and were evaluable for toxicity. A total of 144 cycles were administered. The median number of cycles per patient was 4 (range 1–12). Two patients (7%) received 12 cycles, the maximum

number of cycles allowed per protocol. Ten patients (35%) required dose modifications (ANC, neuropathy, or weakness); 6 (26%) in phase 1 and 4 (66%) in phase 1b. Of the patients who received dose modifications, 5 (50%) received a dose reduction with docetaxel alone, 1 (10%) with satraplatin alone, and 4 (40%) with a combination of docetaxel and satraplatin. Treatment was delayed in 35 cycles (24%) by a median of 7 days (range 1–20). The reasons for delay were patient request (7 cycles), scheduling (15 cycles), poor performance status (2 cycles), urinary complications (1 cycle), infection (2 cycle), grade 3 thrombocytopenia (1 cycle), grade 4 neutropenia (1 cycle), grade 1 anemia (1 cycle), hyponatremia (1 cycle), MD discretion (1 cycle), elevated AST (1 cycle), and dental procedures (2 cycles).

3.3. Safety

Treatment-related toxicity for the entire cohort is detailed in Table 3. Neutropenia was the most common treatment-related hematologic toxicity. Fatigue, alopecia, and GI complaints were the most common nonhematologic toxicities. There were no grade 4 nonhematologic toxicities reported. There were no treatment-related deaths.

3.4. Responses

In total, 25 patients were evaluable for disease according to RECIST: 22 (96%) in phase 1 and 3 (50%) in dose 1b portion of the trial. Their results are listed in Table 4. The overall response rate (complete response and partial response) for this study was 16% (95% CI: 6%–35%). The 4 patients who achieved a response all had adenocarcinoma of the prostate. Of the 6 patients treated with docetaxel and satraplatin as first line treatment in the phase 1b, 3 (50%) demonstrated >50% decline in their prostate specific antigen (PSA) levels.

The reasons for treatment discontinuation were varied. Twelve (41%) patients discontinued treatment due to disease progression, 6 (21%) at the discretion of the physician due to signs of clinical progression, 6 (21%) due to the achievement of maximum benefit, 3 (10%) due to hematologic toxicity (thrombocytopenia), and 2 (7%) per patient wishes.

4. Discussion

Platinum-based chemotherapy is active in several solid tumors including lung, head and neck, colon, bladder, ovarian, and testicular cancers. The traditional platinum agents, cisplatin, carboplatin, and oxaliplatin are all administered intravenously and are associated in varying degrees with neurotoxicity, nephrotoxicity, myelosuppression, and ototoxicity. Satraplatin, an oral platinum, has convenient dosing and in phase 1 testing was not associated with neurotoxicity, nephrotoxicity, or ototoxicity [6–9]. For these reasons it is an attractive candidate for clinical applications.

In phase 1 testing, linear pharmacokinetics were noticed with a daily 5-day dosing schedule, repeating every 3–4 weeks [7]. The primary dose limiting was myelosuppression, although this recovered by day 28. Another phase 1 study used satraplatin in combination with paclitaxel in patients with advanced malignancies [20]. In that study, satraplatin for 5 days and paclitaxel on day 1 repeated every 21 days was used and, in general, the combination was tolerable with neutropenia being the most frequent side effect. They reported an overall response rate of 21%, stable disease in 24%, and progression disease in 42%.

In the phase III trial, satraplatin and prednisone against refractory cancer (SPARC) trial, men with metastatic castrate resistant prostate cancer who were previously treated with at least 1 chemotherapy regimen, were randomized to either satraplatin 80 mg/m² days 1–5 of a 35-day cycle plus prednisone vs. prednisone plus placebo [21]. The primary end points were progression-free survival and overall survival. The trial did not demonstrate a survival

benefit for the population receiving satraplatin compared with placebo (median overall survival 61.3 weeks for satraplatin vs. 61.4 weeks for placebo, HR = 0.98). As a result, satraplatin was not approved for second-line use in metastatic CRPC.

However, the SPARC trial did demonstrate an improvement in a composite progression-free survival end point (11.1 weeks for satraplatin vs. 9.7 weeks for placebo, $P < 0.001$), an increased time to progression, a reduction in pain response, and an improvement in PSA response. Since the trial was initiated in 2003 before docetaxel became the standard first line option for metastatic CRPC, only half (51%) of the patients received prior docetaxel therapy. A prespecified analysis of docetaxel-pretreated patients demonstrated improved median overall survival with satraplatin compared with placebo (66.1 weeks vs. 62.9 weeks, $P = 0.039$).

The current trial builds on this experience by combining satraplatin with docetaxel in patients with advanced malignancies with an expansion cohort of chemotherapy naïve metastatic castrate resistant prostate cancer patients. After completion of the phase 1 portion, we then proceeded to define the recommended phase 2 dose in combination with prednisone in patients with metastatic CRPC.

Overall, the combination of satraplatin and docetaxel was well tolerated. Ten (35%) of the patients required dosage modifications due to toxicity; 24% of cycles were delayed, but the most common reason was scheduling related (43%). Similar to other trials using satraplatin, the most common toxicity was hematologic; 86% of the patients experienced grade 1–4 neutropenia and leukopenia, while 52% experienced grade 1–4 anemia. For the phase 1 portion of the trial, 4 disease-limiting toxicities were noted and all them were related to grade 3/4 neutropenia. The most common non-hematologic toxicities were nausea, vomiting, fatigue, and alopecia. There were no reported grade 4 non-hematologic toxicities in any of the cycles, and grade 3 non-hematologic toxicity was uncommon. The recommended phase 2 dose was docetaxel 60 mg/m² i.v. day 1 with satraplatin 40 mg/m² PO days 1–5, without G-CSF support, repeated in 3-week cycles. With G-CSF support, the recommended phase II dose was docetaxel 70 mg/m² i.v. day 1 with satraplatin 50 mg/m² PO days 1–5 repeated in 3-week cycles. For patients with metastatic CRPC, the recommended phase 2 dose of docetaxel 75mg/m² i.v. day 1 with satraplatin 50 mg/m²/day PO days 1–5, with G-CSF and prednisone 10 mg daily, repeated in 3-week cycles appeared safe with no DLTs noted.

The overall response rate (complete response and partial response) for this study was 16% (95% CI: 6%–35%). Fifty-two percent of the patients achieved stable disease. The PSA response in the phase 1b, as defined by 50% decline in PSA, was 50%.

While satraplatin alone failed to extend the median overall survival in the SPARC trial, the results of this study establish that the combination of satraplatin and docetaxel was well tolerated and safe. Based on this preliminary data, the combination appeared active and, therefore, may warrant further evaluation in selected patient populations. If future studies utilize this combination, we recommend the routine use of G-CSF to minimize hematologic toxicity.

5. Conclusion

The combination of satraplatin and docetaxel is feasible with neutropenia as the main toxicity and, therefore, requires the use of G-CSF in a heavily pretreated population. The future use of satraplatin either alone or in combination with other agents is unclear.

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References

- [1]. Kelland LR. An update on satraplatin: The first orally available platinum anticancer drug. *Expert Opin Investig Drugs*. 2000; 9:1373–82.
- [2]. Mellish KJ, Barnard CF, Murrer BA, et al. DNA-binding properties of novel cis- and trans-platinum-based anticancer agents in 2 human ovarian carcinoma cell lines. *Int J Cancer*. 1995; 62:717–23. [PubMed: 7558420]
- [3]. Fokkema E, Groen HJ, Helder MN, et al. JM216-, JM118-, and cisplatin-induced cytotoxicity in relation to platinum-DNA adduct formation, glutathione levels and p53 status in human tumor cell lines with different sensitivities to cisplatin. *Biochem Pharmacol*. 2002; 63:1989–96. [PubMed: 12093475]
- [4]. Kelland LR, Abel G, McKeage MJ, et al. Preclinical antitumor evaluation of bis-acetato-ammine-dichloro-cyclohexylamine platinum (IV): An orally active platinum drug. *Cancer Res*. 1993; 53:2581–6. [PubMed: 8388318]
- [5]. Twentyman PR, Wright KA, Mistry P, et al. Sensitivity to novel platinum compounds of panels of human lung cancer cell lines with acquired and inherent resistance to cisplatin. *Cancer Res*. 1992; 52:5674–80. [PubMed: 1327513]
- [6]. McKeage MJ, Mistry P, Ward J, et al. A phase I and pharmacology study of an oral platinum complex, JM216: Dose-dependent pharmacokinetics with single-dose administration. *Cancer Chemother Pharmacol*. 1995; 36:451–8. [PubMed: 7554035]
- [7]. McKeage MJ, Raynaud F, Ward J, et al. Phase I and pharmacokinetic study of an oral platinum complex given daily for 5 days in patients with cancer. *J Clin Oncol*. 1997; 15:2691–700. [PubMed: 9215842]
- [8]. Beale P, Raynaud F, Hanwell J, et al. Phase I study of oral JM216 given twice daily. *Cancer Chemother Pharmacol*. 1998; 42:142–8. [PubMed: 9654114]
- [9]. Sessa C, Minoia C, Ronchi A, et al. Phase I clinical and pharmacokinetic study of the oral platinum analogue JM216 given daily for 14 days. *Ann Oncol*. 1998; 9:1315–22. [PubMed: 9932162]
- [10]. Wosikowski K, Lamphere L, Unteregger G, et al. Preclinical antitumor activity of the oral platinum analog satraplatin. *Cancer Chemother Pharmacol*. 2007; 60:589–600. [PubMed: 17541592]
- [11]. Judson I, Cerny T, Epelbaum R, et al. Phase II trial of the oral platinum complex JM216 in non-small-cell lung cancer: An EORTC early clinical studies group investigation. *Ann Oncol*. 1997; 8:604–6. [PubMed: 9261531]
- [12]. Fokkema E, Groen HJ, Bauer J, et al. Phase II study of oral platinum drug JM216 as first-line treatment in patients with small-cell lung cancer. *J Clin Oncol*. 1999; 17:3822–7. [PubMed: 10577855]
- [13]. Trudeau M, Stuart G, Hirte H, et al. A phase II trial of JM-216 in cervical cancer: An NCIC CTG study. *Gynecol Oncol*. 2002; 84:327–31. [PubMed: 11812095]
- [14]. Latif T, Wood L, Connell C, et al. Phase II study of oral bis (aceto) ammine dichloro (cyclohexamine) platinum (IV) (JM-216, BMS-182751) given daily $\times$ 5 in hormone refractory prostate cancer (HRPC). *Invest New Drugs*. 2005; 23:79–84. [PubMed: 15528984]
- [15]. Sternberg CN, Whelan P, Hetherington J, et al. Phase III trial of satraplatin, an oral platinum plus prednisone vs. prednisone alone in patients with hormone-refractory prostate cancer. *Oncology*. 2005; 68:2–9. [PubMed: 15741753]
- [16]. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med*. 2004; 351:1502–12. [PubMed: 15470213]

- [17]. Petrylak DP, Tangen CM, Hussain MH, et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med*. 2004; 351:1513–20. [PubMed: 15470214]
- [18]. Lamphere L, Obermayr F, Caligiuri M, et al. Satraplatin, an oral platinum analog, is active and synergistic with paclitaxel and docetaxel in prostate carcinoma models. *J Clin Oncol* [Meeting Abstract]. 2006; 24:14620.
- [19]. Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. *J Natl Cancer Inst*. 2000; 92:205–16. [PubMed: 10655437]
- [20]. Thompson DS, Spigel DR, Hainsworth JD, et al. Phase II trial of satraplatin (S) and paclitaxel (P) in first-line advanced non-small-cell lung cancer (NSCLC) treatment: Final results. *J Clin Oncol* [Meeting Abstracts]. 2008; 26:19023.
- [21]. Sternberg CN, Petrylak DP, Sartor O, et al. Multinational, double-blind, phase III study of prednisone and either satraplatin or placebo in patients with castrate-refractory prostate cancer progressing after prior chemotherapy: The SPARC trial. *J Clin Oncol*. 2009; 27:5431–8. [PubMed: 19805692]

Table 1Patient demographics and baseline disease characteristics ($n = 29$)

Characteristic	No. of patients	%
Sex		
Male	22	76
Female	7	24
Race		
White	29	100
Age (y) median, (range)	65 (48–80)	
ECOG performance status		
0	8	28
1	20	69
2	1	3
Diagnosis		
Prostate	18	62
Pancreas	3	10
Esophageal	2	7
Breast	2	7
Bladder	2	7
Head and neck	2	7
Previous number of cytotoxics		
0*	13	45
1	8	28
2	5	17
3	2	7
4	1	3
Site of metastases		
Bone	20	69
Lymph nodes	12	41
Liver	9	31
Lung	7	24
Other**	1	3

ECOG = Eastern Cooperative Oncology Group.

* No patient in the dose expansion cohort received prior cytotoxic therapies.

** Other sites: oral cavity.

Table 2

Dose escalation and DLTs (phase 1 and 1b)

Dose level	Docetaxel (mg/m ²)	Satraplatin (mg/m ²)	G-CSF	No. of patients	No. of cycles	DLT	Type of DLT
-1	60	40	No	6	28	1	ANC
1	60	50	No	7	29	2	ANC
2	60	50	Yes	3	18	0	—
3	70	50	Yes	7	27	1	ANC
4*	60	50	Yes	3	20	0	—
5*	75	50	Yes	3	22	0	—

G-CSF = granulocyte colony stimulating factor.

*Phase 1b portion, which included the use of prednisone 10 mg daily.

Table 3Adverse events observed in at least 10% of patients ($n = 29$)

Toxicity	Grade 1–2	Grade 3	Grade 4	%Occurrence
Hematologic				
Neutropenia	19	22	21	86
Leukopenia	18	20	10	86
Thrombocytopenia	7	1	1	24
Anemia	15	3	0	52
Nonhematologic				
Fatigue	24	2	0	90
Diarrhea	22	1	0	79
Nausea	20	1	0	72
Alopecia	16	0	0	55
Constipation	9	2	0	40
Dizziness	10	0	0	34
Anorexia	9	1	0	34
Vomiting	8	1	0	31
Muscle weakness/ pain	6	3	0	31
Dyspepsia	7	1	0	28
Neuropathy	6	0	0	21
Edema	6	0	0	21
Respiratory complaints	6	0	0	21
Rash	5	0	0	17
Infection	2	2	0	14
Abdominal pain	3	0	0	10
Arthralgias	3	0	0	10
Stomatitis	3	0	0	10
Epistaxis	3	0	0	10
Fever	3	0	0	10

Table 4Responses for patients with measurable disease ($n = 25$)

Response ^a	No. of patients (%)	95% Confidence interval ^b
CR	0 (0)	0%–13%
PR	4 (16)	6%–35%
SD	13 (52)	33%–70%
PD	8 (32)	17%–52%

^aCR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; based on RECIST.

^bExact binomial confidence interval.