The Oncologist®

Clinical Trial Results

Randomized Phase II Study of Cabazitaxel Versus Methotrexate in Patients With Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck Previously Treated With Platinum-Based Therapy

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Disclosures of potential conflicts of interest may be found at the end of this article.

Trial Information

- **ClinicalTrials.gov Identifier:** NCT01528163
- **Sponsor:** Cliniques Universitaires Saint-Luc
- **Principal Investigator:** Jean-Pascal Henry Machiels
- **IRB Approved:** Yes

Lessons Learned

- Cabazitaxel has activity in squamous cell carcinoma of the head and neck (SCCHN) and taxane-resistant cell lines. For the first time, cabazitaxel was investigated in incurable patients with recurrent SCCHN. Patients were randomly assigned to cabazitaxel every 3 weeks or weekly methotrexate.
- This phase II study did not meet its primary endpoint.
- Cabazitaxel has low activity in SCCHN.
- The toxicity profile in this population also was not favorable owing to the high rate of febrile neutropenia observed (17%).

Abstract

Background. Cabazitaxel is a second-generation taxane that improves the survival of patients with metastatic castrate-resistant prostate cancer following docetaxel therapy. Cabazitaxel has activity in squamous cell carcinoma of the head and neck (SCCHN) and taxane-resistant cell lines. In this randomized phase II trial, we investigated cabazitaxel in patients with recurrent SCCHN.

Methods. Patients with incurable SCCHN with progression after platinum-based therapy were randomly assigned to cabazitaxel every 3 weeks (cycle 1, 20 mg/m^2, increased to 25 mg/m^2 for subsequent cycles in the absence of non-hematological adverse events [AEs] greater than grade 2 and hematological AEs greater than grade 3) or methotrexate (40 mg/m^2/week). The patients were stratified according to their performance status and previous platinum-based chemotherapy for palliation versus curative intent. The primary endpoint was the progression-free survival rate (PFSR) at 18 weeks.

Results. Of the 101 patients, 53 and 48, with a median age of 58.0 years (range, 41–80), were randomly assigned to cabazitaxel

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or methotrexate, respectively. The PFSR at 18 weeks was 13.2% (95% confidence interval [CI], 5%–25%) for cabazitaxel and 8.3% (95% CI, 2%–20%) for methotrexate. The median progression-free survival was 1.9 months in both arms. The median overall survival was 5.0 and 3.6 months for cabazitaxel and methotrexate, respectively. More patients experienced serious adverse events with cabazitaxel than with methotrexate (54% vs. 36%). The most common drug-related grade 3–4 AE in the cabazitaxel arm was febrile neutropenia (17.3%).

Conclusion. This study did not meet its primary endpoint. Cabazitaxel has low activity in recurrent SCCHN. ***The Oncologist*** 2016;21:1416–e17

Discussion

The activity observed with cabazitaxel was similar to that of methotrexate, with the exception of the rate of stable disease (SD) at 9 weeks, which was higher in the cabazitaxel arm than in the methotrexate arm: 32% versus 14.6%. The median PFS and overall survival observed in the cabazitaxel and methotrexate arms were comparable to the other single-agent palliative studies performed in the same setting. Another nonrandomized study (UNICANCER ORL03) investigated cabazitaxel in patients with recurrent SCCHN. The rate of SD (primary endpoint) at 6 weeks was 27.6% (95% CI, 12.7%–47.2%), within the same range as that observed in the present study. Twenty-nine percent of our patients ($n = 21$) previously exposed to taxanes had SD with cabazitaxel. Therefore, the rate of disease stabilization with cabazitaxel does not seem to be influenced by previous exposure to taxane-based therapies.

A striking observation was the high rate of grade 3–4 neutropenia (48%) and febrile neutropenia (17.3%) in the cabazitaxel arm. The rate of febrile neutropenia in the UNICANCER SCCHN study, which investigated cabazitaxel at 25 mg/m^2 every 3 weeks, was 26%, despite primary prophylaxis with granulocyte-colony stimulating factor. In contrast to the UNICANCER study, primary prophylaxis was not initially mandatory in our trial; however, the initial dose of cabazitaxel was lower (20 mg/m^2 every 3 weeks) and was only increased to 25 mg/m^2 in the absence of nonhematological AEs higher than grade 2 and hematological AEs higher than grade 3 during the first cycle. Nevertheless, we observed a high rate of febrile neutropenia even after the amendment that made the use of pegfilgrastim mandatory as primary prophylaxis. The rate of febrile neutropenia observed in these two SCCHN studies was higher than previously reported in the TROPIC trial (8%). In contrast to the TROPIC trial, we did not observe any treatment-related deaths or grade 3 diarrhea, perhaps owing to the lower cabazitaxel dose.

In conclusion, cabazitaxel monotherapy has no clinically meaningful activity in patients with recurrent SCCHN who develop progression after platinum therapy. The toxicity profile in this population also was not favorable owing to the high rate of febrile neutropenia observed.

Trial Information

Disease	Head and neck cancers
Stage of disease / treatment	Metastatic / advanced
Prior therapy	1 prior regimen
Type of study - 1	Phase II
Type of study - 2	Randomized
ORR	P: 0
PFS	P: 1.9
Primary endpoint	Progression-free survival
Secondary endpoint	Overall response rate
Secondary endpoint	Overall survival
Secondary endpoint	Toxicity
Additional details of endpoints or study design	

Inclusion and Exclusion Criteria

Eligible patients were required to have recurrent squamous cell carcinoma of the head and neck (SCCHN), Eastern Cooperative Oncology Group performance status (ECOG PS) 0–2, disease not amenable to curative treatment, and at least one measurable lesion according to the Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST). Progressive disease (PD) within 1 year after first-line platinum-based chemotherapy, given either as part of multimodal curative treatment or in the palliative setting, was also required. Patients were required to have adequate organ function, absolute neutrophil count $>$1,500/mm^3, hemoglobin $\geq$9 g/dL, platelet count $>$100,000/mm^3, serum creatinine $\leq$1.5 the upper limit of normal (ULN), total bilirubin $<$1 ULN, and alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT) $<$1.5 ULN.

Patients were excluded if they had nasopharyngeal carcinoma, known brain metastases, previous malignancy from which the patient has been disease-free for $<$5 years (other than SCCHN), active grade $>$2 peripheral neuropathy, active grade $>$2 stomatitis, a history of severe hypersensitivity reaction (grade $>$3) to polysorbate 80-containing drugs, or any other serious illness or medical conditions. Patients were also ineligible if they had received previous cabazitaxel, more than two previous lines of chemotherapy in the palliative setting, or radiation therapy or surgery or investigational drugs within 4 weeks of the study. Previous administration of anti-epidermal growth factor receptor therapy or docetaxel or paclitaxel was allowed in the curative or palliative setting.

The study was approved by the independent ethics committee and the Belgian and Luxembourg Health Authorities and conducted in accordance with the Declaration of Helsinki (October 2000). All the patients provided written informed consent.

Study Endpoints and Outcome
The primary endpoint was the progression-free survival rate (PFSR) at 18 weeks, defined as the proportion of patients alive and free of progression according to the RECIST at 18 weeks after treatment. The secondary endpoints were toxicity, objective response rate (ORR), progression-free survival (PFS), and overall survival (OS).

Side effects were recorded according to the National Cancer Institute Common Toxicity Criteria (NCI-CTI), version 4. Treatment emergent adverse events were defined as events that occurred after study treatment initiation or that had worsened relative to the pretreatment state. PFS was defined as the time interval between the date of randomization and the date of disease progression or the date of death from any cause. For patients who did not experience an event (i.e., those lost to follow-up or those without progression at the date of data cutoff), PFS was censored. OS was defined as the time interval between the date of randomization until death from any cause or until the date of the last follow-up visit. The survival time was censored on the last date the patient was known to be alive. The best overall response was assessed according to the RECIST. ORR was defined as the proportion of patients with a complete response or partial response (PR). Patients with unknown or missing response data were treated as nonresponders. The relative dose intensity of cabazitaxel and methotrexate was calculated as being equal to the dose intensity divided by the planned dose intensity, multiplied by 100.

Study Design
The present study was an open-label, noncomparative, multicenter, international randomized phase II study (ClinicalTrials.gov identifier, NCT01528163). Eligible patients were randomly assigned to cabazitaxel (20 mg/m^2 every 3 weeks) or methotrexate (40 mg/m^2 weekly). The dose of cabazitaxel was increased to 25 mg/m^2 for the second and subsequent cycles in the absence of nonhematological adverse events (AEs) greater than grade 2 and hematological AEs greater than grade 3 during the first cycle. The use of pegfilgrastim was initially at the discretion of the investigator but became mandatory as primary prophylaxis following the interim safety analysis performed by the independent data monitoring committee. The interim analysis was performed after 39 patients (21 and 18 in the cabazitaxel and methotrexate arms, respectively) had completed treatment. Treatment allocation was performed using minimization. The two stratification parameters were ECOG PS 0–1 versus 2 and previous platinum-based chemotherapy for palliation versus curative intent. Cabazitaxel was continued until PD, unacceptable toxicity, or a maximum 10 cycles. Methotrexate was continued until PD or unacceptable toxicity.

Pretreatment Evaluation and Follow-Up
Pretreatment examinations were performed within 2 weeks before the start of treatment and included complete history, physical examination, chest and abdominal computed tomography (CT), cervical imaging by magnetic resonance or CT, and 12-lead electrocardiography. Weekly laboratory tests for both arms included hemoglobin, white blood cell count (neutrophils), and platelets. Tests for bilirubin, ALAT, ASAT, and electrolytes (glucose, sodium, potassium, and chloride) were performed before each infusion. Imaging was repeated every 9 weeks. Imaging for tumor evaluation was centrally reviewed (J.S.).

Statistical Analysis
The experimental group (cabazitaxel) was designed according to the Fleming single-stage test procedure. The trial was to be considered positive if the results were consistent with a true PFSR at 18 weeks of 30% or more but would be rejected if the PFSR at the same time point was 15% or less (Po = .15, P1 = .30, type I error = 0.1, type II error = 0.1). According to these hypotheses, 49 eligible patients needed to be recruited to the cabazitaxel arm. At least 11 patients were required to achieve SD or a PR at 18 weeks after treatment for the study to meet its primary endpoint.

To obtain the necessary number of assessable patients, 53 patients were enrolled in the cabazitaxel arm with the assumption that 10% of these patients would not be assessable for the primary endpoint. The aim of randomization was to offer a valid internal control group by avoiding a possible selection bias with no intention of comparing the two arms. Because randomization was performed by blocks, the study was stopped after the inclusion of 53 patients in the cabazitaxel arm. At that point, 48 patients were included in the methotrexate arm. The Kaplan-Meier method was used to estimate the median PFS and OS times.

Investigator's analysis	Level of activity did not meet planned endpoint

Drug Information Control Arm

Drug 1	
Generic/working name	Methotrexate
Dose	40 mg/m^2
Route	i.v.
Schedule of administration	40 mg/m^2 weekly i.v.

Drug Information Experimental Arm

Drug 1	
Generic/working name	Cabazitaxel
Dose	20 mg/m^2
Route	i.v.
Schedule of administration	Cabazitaxel (20 mg/m^2 every 3 weeks). The dose of cabazitaxel was increased to 25 mg/m^2 for the second and subsequent cycles in the absence of nonhematological AEs greater than grade 2 and hematological AEs greater than grade 3 during the first cycle.

Patient Characteristics	
Number of patients, male	84
Number of patients, female	17
Stage	Noncurable recurrent/metastatic
Age	Median (range): 58 (41–80)
Number of prior systemic therapies	Median (range): 1 (0–2)
Performance status: ECOG	0 — 1 — 84 2 — 17 3 — 0 Unknown —
Cancer types or histologic subtypes	Squamous cell carcinoma of the head and neck: 101

Primary Assessment Method	
Control arm: squamous cell carcinoma of the head and neck (methotrexate)	
Number of patients screened	48
Number of patients enrolled	48
Number of patients evaluable for toxicity	45
Number of patients evaluated for efficacy	48
Response assessment CR	$n = 0$ (0)
Response assessment PR	$n = 0$ (0)
Response assessment SD	$n = 7$ (14.6)
(Median) duration assessments PFS	1.9 months, 95% CI: 1.5–2.1
(Median) duration assessments OS	3.6 months, 95% CI: 2.7–6.2
Kaplan-Meier time units	Months

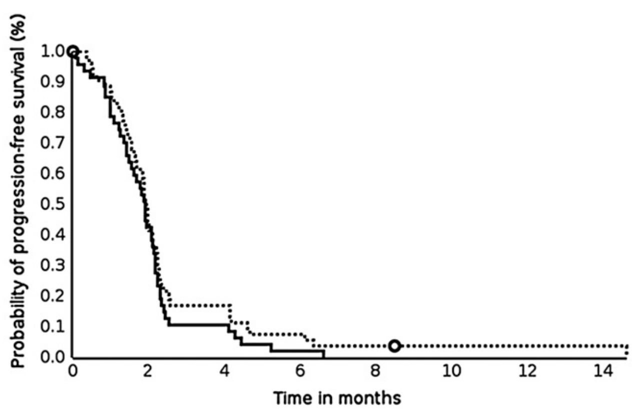
Time of scheduled assessment and/or time of event	No. progressed (or deaths)	No. censored	Percentage at start of evaluation period	Kaplan-Meier %	No. at next evaluation/no. at risk
0.0000	0	1	100.00	100.00	47
0.0658	1	0	100.00	97.87	46
0.1316	1	0	97.87	95.74	45
0.2961	1	0	95.74	93.62	44
0.4605	1	0	93.62	91.49	43
0.8224	1	0	91.49	89.36	42
0.8553	2	0	89.36	85.11	40
0.9868	3	0	85.11	78.72	37
1.0855	1	0	78.72	76.60	36
1.2171	1	0	76.60	74.47	35
1.25	1	0	74.47	72.34	34
1.3487	1	0	72.34	70.21	33
1.4145	2	0	70.21	65.96	31
1.4803	1	0	65.96	63.83	30
1.5461	1	0	63.83	61.70	29
1.6118	1	0	61.70	59.57	28
1.6776	1	0	59.57	57.45	27
1.7763	1	0	57.45	55.32	26
1.8092	1	0	55.32	53.19	25
1.8750	1	0	53.19	51.06	24
1.9079	3	0	51.06	44.68	21
1.9408	1	0	44.68	42.55	20
2.0724	2	0	42.55	38.30	18
2.1053	1	0	38.30	36.17	17
2.1382	1	0	36.17	34.04	16

2.1711	3	0	34.04	27.66	13
2.2368	2	0	27.66	23.40	11
2.3026	2	0	23.40	19.15	9
2.3355	1	0	19.15	17.02	8
2.4013	1	0	17.02	14.89	7
2.4342	1	0	14.89	12.77	6
2.5329	1	0	12.77	10.64	5
4.1118	1	0	10.64	8.51	4
4.2763	1	0	8.51	6.38	3
4.4408	1	0	6.38	4.26	2
5.2303	1	0	4.26	2.13	1
6.6118	1	0	2.13	0.00	0

Experimental Arm: Squamous Cell Carcinoma of the Head and Neck (Cabazitaxel)	
Number of patients screened	53
Number of patients enrolled	53
Number of patients evaluable for toxicity	52
Number of patients evaluated for efficacy	53
Response assessment CR	$n = 0$ (0)
Response assessment PR	$n = 0$ (0)
Response assessment SD	$n = 17$ (32)
(Median) duration assessments PFS	1.9 months, 95% CI: 1.6–2.1
(Median) duration assessments OS	5 months, 95% CI: 3.6–6
Kaplan-Meier time units	Months

Time of scheduled assessment and/or time of event	No. progressed (or deaths)	No. censored	Percentage at start of evaluation period	Kaplan-Meier %	No. at next evaluation/no. at risk
0.0000	0	0	100.00	100.00	53
0.3618	1	0	100.00	98.11	52
0.4276	1	0	98.11	96.23	51
0.4934	1	0	96.23	94.34	50
0.5263	1	0	94.34	92.45	49
0.6250	1	0	92.45	90.57	48
0.8224	1	0	90.57	88.68	47
0.9868	1	0	88.68	86.79	46
1.0197	1	0	86.79	84.91	45
1.0855	1	0	84.91	83.02	44
1.2171	1	0	83.02	81.13	43
1.2829	1	0	81.13	79.25	42
1.3158	1	0	79.25	77.36	41
1.3816	1	0	77.36	75.47	40
1.4145	1	0	75.47	73.58	39
1.4474	1	0	73.58	71.70	38
1.5461	2	0	71.70	67.92	36
1.6118	1	0	67.92	66.04	35
1.6447	1	0	66.04	64.15	34
1.6776	1	0	64.15	62.26	33
1.7763	1	0	62.26	60.38	32
1.8421	1	0	60.38	58.49	31
1.8750	3	0	58.49	52.83	28
1.9079	1	0	52.83	50.94	27
1.9408	1	0	50.94	49.06	26
1.9737	3	0	49.06	43.40	23

2.0066	1	0	43.40	41.51	22
2.1053	3	0	41.51	35.85	19
2.2039	1	0	35.85	33.96	18
2.2368	2	0	33.96	30.19	16
2.2697	2	0	30.19	26.42	14
2.3026	1	0	26.42	24.53	13
2.3355	1	0	24.53	22.64	12
2.4671	1	0	22.64	20.75	11
2.5329	1	0	20.75	18.87	10
2.5658	1	0	18.87	16.98	9
4.1447	2	0	16.98	13.21	7
4.1776	1	0	13.21	11.32	6
4.6053	1	0	11.32	9.43	5
4.6711	1	0	9.43	7.55	4
6.1184	1	0	7.55	5.66	3
6.3487	1	0	5.66	3.77	2
8.4868	0	1	3.77	3.77	1
14.6053	1	0	3.77	0.00	0



Number at Risk—control	47	46	45	44	43	43	40	37	36	35	34	33	31	30	29	28	27	26	25	24	21	20
Number Censored—control	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Number at Risk—experimental	53	52	51	50	49	48	47	46	45	44	43	42	41	40	39	38	36	35	34	33	32	31
Number Censored—experimental	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Number at Risk—control	18	17	16	13	11	9	8	7	6	5	4	3	2	1	0							
Number Censored—control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
Number at Risk—experimental	28	27	26	23	22	19	18	16	14	13	12	11	10	9	7	6	5	4	3	2	1	0
Number Censored—experimental	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0

Kaplan-Meier plot. PFS probabilities (central review). Dotted line: cabazitaxel; solid line: methotrexate.

Control Arm: Total Patient Population (Methotrexate)

Response assessment CR	$n = 0$ (0)
Response assessment PR	$n = 0$ (0)

Experimental Arm: Total Patient Population (Cabazitaxel)

Response assessment CR	$n = 0$ (0)
Response assessment PR	$n = 0$ (0)

Adverse Events Control Arm (Methotrexate): All Cycles

Name	*NC/NA	1	2	3	4	5	All Grades
Diarrhea	96%	4%	0%	0%	0%	0%	4%
Weight loss	96%	4%	0%	0%	0%	0%	4%
Fatigue	92%	4%	2%	2%	0%	0%	8%
Mucositis oral	82%	8%	2%	8%	0%	0%	18%
Nausea	96%	4%	0%	0%	0%	0%	4%
Anemia	34%	31%	33%	2%	0%	0%	66%

Neutrophil count decreased	86%	8%	2%	4%	0%	0%	14%
Platelet count decreased	67%	29%	0%	2%	2%	0%	33%

Adverse Events Legend
Treatment emergent adverse events occurring in more than 5% in the methotrexate group.
*No Change From Baseline/No Adverse Event

Serious Adverse Events Control Arm (Methotrexate)

Name	Grade	Attribution
Thrombocytopenia	4	Probable

Adverse Events Experimental Arm (Cabazitaxel): All Cycles

Name	*NC/NA	1	2	3	4	5	All Grades
Weight loss	94%	2%	4%	0%	0%	0%	6%
Fatigue	79%	13%	4%	4%	0%	0%	21%
Diarrhea	86%	8%	6%	0%	0%	0%	14%
Mucositis oral	90%	8%	2%	0%	0%	0%	10%
Nausea	92%	8%	0%	0%	0%	0%	8%
Anemia	11%	25%	62%	2%	0%	0%	89%
Neutrophil count decreased	12%	30%	11%	17%	30%	0%	88%
Platelet count decreased	58%	34%	4%	2%	2%	0%	42%
Febrile neutropenia	83%	0%	0%	9%	8%	0%	17%

Adverse Events Legend
Treatment emergent adverse events occurring in more than 5% in the cabazitaxel group.
*No Change From Baseline/No Adverse Event

Serious Adverse Events Experimental Arm (Cabazitaxel)

Name	Grade	Attribution
Febrile neutropenia	3	Definite
Febrile neutropenia	4	Definite

Assessment, Analysis, and Discussion

Completion	Study completed
Pharmacokinetics / Pharmacodynamics	Not Collected
Investigator's Assessment	Level of activity did not meet planned endpoint.

We report the results of the first clinical trial to investigate cabazitaxel in SCCHN. Cabazitaxel monotherapy was found to have modest clinical activity in recurrent and/or metastatic SCCHN with a PFSR at 18 weeks of 13.2%. The median PFS and OS were 1.9 months and 5 months, respectively. Thirty-two percent of patients achieved SD at the first tumor evaluation, but no ORRs were recorded.

The activity observed with cabazitaxel was similar to that of methotrexate in this study, with the exception of the rate of SD at 9 weeks, which was higher in the cabazitaxel arm than in the methotrexate arm: 32% versus 14.6%. The median PFS and OS observed in the cabazitaxel and methotrexate arms were comparable to those of other single-agent palliative studies performed in the same setting [1–5]. The baseline characteristics of our patients did not seem to explain the poor outcomes observed: only 17% of the patients had ECOG PS 2, and 19% had received two previous lines of chemotherapy for recurrent disease. Another nonrandomized study (UNICANCER ORL03), reported as an abstract, investigated cabazitaxel in patients with recurrent SCCHN [6]. The rate of SD (primary endpoint) at 6 weeks was 27.6% (95% CI, 12.7%–47.2%), within the same range as that observed in the present study (30.2%; 95% CI, 19.9%–46.3%). Their study population was, however, more heavily pretreated, as all patients were required to have progression after platinum, cetuximab, and taxane therapy to meet the eligibility criteria. Twenty-nine percent of our patients ($n = 21$) previously exposed to taxanes had SD with cabazitaxel. Therefore, the rate of disease stabilization with cabazitaxel does not seem to be influenced by previous exposure to taxane-based therapies. Human papillomavirus (HPV) and p16 have been linked to a favorable prognosis in recurrent and/or metastatic SCCHN. Because of the low number of patients in the present trial, p16 and HPV status were not assessed. The PFSR at 18 weeks for the relapsing oropharyngeal cancer patients treated with cabazitaxel was 28.6% (95% CI, 9.4%–58.1%). However, the low number of patients ($n = 13$) included in this subset analysis did not allow any definitive conclusions to be drawn.

The higher rate of an objective response reported in trials evaluating docetaxel and paclitaxel in SCCHN was generally obtained in less heavily pretreated patients [7–10]. Therefore, we cannot exclude the potential for cabazitaxel to demonstrate

enhanced activity in patients with less-advanced disease. A dose-escalation trial combining cabazitaxel with platinum/5-fluorouracil as induction chemotherapy is ongoing (ClinicalTrials.gov identifier, NCT01379339).

A striking finding of our trial was the high rate of grade 3–4 neutropenia (48%) and febrile neutropenia (17.3%) in the cabazitaxel arm. The rate of febrile neutropenia in the UNICANCER SCCHN study that investigated cabazitaxel at 25 mg/m^2 every 3 weeks was 26%, despite primary prophylaxis with granulocyte-colony stimulating factor [6]. In contrast to the UNICANCER study, primary prophylaxis was not initially mandatory in our trial but the initial dose of cabazitaxel was lower (20 mg/m^2 every 3 weeks) and was only increased to 25 mg/m^2 in the absence of nonhematological AEs higher than grade 2 and hematological AEs higher than grade 3 during the first cycle. Nevertheless, we observed a high rate of febrile neutropenia even after the amendment that made the use of pegfilgrastim mandatory as primary prophylaxis. The rate of febrile neutropenia observed in these two SCCHN studies was higher than previously reported in the TROPIC trial (8%) [11].

Two dose-escalation studies investigated cabazitaxel administered every 3 weeks [12, 13]. The dose-limiting toxicities were neutropenia and diarrhea. The cabazitaxel dose recommended for further clinical trials was 20 or 25 mg/m^2 every 3 weeks. In the TROPIC trial, which demonstrated that cabazitaxel improved OS in metastatic castrate-resistant prostate cancer (mCRPC), the dose of cabazitaxel was 25 mg/m^2 every 3 weeks. The most common adverse events associated with cabazitaxel were grade 3 or higher neutropenia, leukopenia, anemia, and febrile neutropenia, occurring in 82%, 68%, 11%, and 8% of patients, respectively. In addition, 6% of the patients developed grade 3 diarrhea, and 5% died of cabazitaxel-related causes. In contrast to the TROPIC trial, we did not observe any treatment-related deaths or grade 3 diarrhea, perhaps because of the lower cabazitaxel dose. A phase III trial comparing 20 mg/m^2 to 25 mg/m^2 every 3 weeks is ongoing in mCRPC, and the results will help define the more appropriate dose.

In conclusion, cabazitaxel monotherapy has no clinically meaningful activity in patients with recurrent and/or metastatic SCCHN with progression after platinum therapy. The toxicity profile in this population also was not favorable owing to the high rate of febrile neutropenia observed.

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Tables

Table 1. Treatment-emergent adverse events occurring in more than 5% in either treatment group

	Methotrexate ($n = 45$)		Cabazitaxel ($n = 52$)	
TEAE	**Grade 1–2**	**Grade 3–4**	**Grade 1–2**	**Grade 3–4**
Patients with any TEAE, *n* (%)	15 (33.3)	13 (28.9)	30 (57.7)	21 (40.4)
Constitutional TEAE, *n* (%)				
Weight loss	2 (4.4)	0 (0)	3 (5.8)	0 (0)
Fatigue	3 (6.7)	1 (2.2)	9 (17.3)	2 (3.8)
Gastrointestinal TEAE, *n* (%)				
Diarrhea	2 (4.4)	0 (0)	7 (13.5)	0 (0)
Mucositis	5 (11.1)	4 (8.9)	5 (8.6)	0 (0)
Nausea	2 (4.4)	0 (0)	4 (7.7)	0 (0)
Hematological TEAE, *n* (%)				
Anemia	31 (68.9)	1 (2)	46 (88.5)	1 (2)
Neutropenia	5 (11.1)	2 (4.4)	22 (19.2)	25 (48.1)
Thrombocytopenia	14 (31.1)	2 (4.4)	20 (34.6)	2 (3.8)
Febrile neutropenia	0 (0)	0 (0)	0 (0)	9 (17.3)

Abbreviation: TEAE, treatment-emergent adverse event.

Table 2. Treatment activity

Variable	Methotrexate ($n = 48$)	Cabazitaxel ($n = 53$)
PFS at 18 wk (%; 95% CI)		
PFS rate at 18 wk (central review, primary endpoint)	8.3 (2.3–20)	13.2 (5.5–25.3)
PFS rate at 18 wk (investigator assessment)	8.3 (2.3–20)	15.1 (6.7–27.6)
ORR and SD by RECIST, *n* (%; 95% CI)		
ORR (central review)	0 (0; 0.0–6.7)	0 (0; 0.0–7.4)
ORR (investigator assessment)	1 (2.1; 0.1–11.1)	0 (0; 0.0–7.4)
SD (central review)	7 (14.6; 6.1–27.8)	17 (32.1; 19.9–46.3)
SD (investigator assessment)	3 (6; 1.3–7.2)	11 (21; 10.8–34.1)
Median PFS (mo; 95% CI)		
Median PFS (central review)	1.9 (1.5–2.1)	1.9 (1.6–2.1)
Median PFS (investigator assessment)	1.9 (1.5–2.1)	1.9 (1.6–2.1)
Median OS (mo; 95% CI)	3.6 (2.7–6.2)	5 (3.6–6.0)

Abbreviations: CI, confidence interval; ORR, objective response rate; OS, overall survival; PSF, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors, version 1.1; SD, stable disease.

Table 3. Patient characteristics

Baseline characteristic	Methotrexate ($n = 48$)	Cabazitaxel ($n = 53$)
Gender, *n* (%)		
Male	41 (85)	43 (81)
Female	7 (15)	10 (19)
ECOG[a], *n* (%)		
0–1	40 (83)	44 (83)
2	8 (17)	9 (17)
Age (yr)		
Median	57.5	58
Range	41–78	46–80

Primary tumor site, *n* (%)		
Oral cavity	16 (33)	17 (32)
Oropharynx	16 (33)	13 (24)
Larynx	3 (6)	12 (23)
Hypopharynx	12 (25)	10 (19)
Unknown primary	1 (2)	1 (2)
Tumor grade at diagnosis, *n* (%)		
Well-differentiated	10 (21)	10 (19)
Moderately differentiated	25 (52)	25 (47)
Poorly differentiated	5 (10)	11 (21)
Unknown/missing	8 (17)	7 (13)
Location of relapse at inclusion, *n* (%)		
Metastatic alone	14 (29)	19 (36)
Local and/or regional only	18 (37)	21 (40)
Locoregional and metastatic	16 (34)	13 (24)
Primary treatment, *n* (%)		
Surgery	29 (60)	30 (57)
Radiation therapy	48 (100)	43 (81)
Chemotherapy		
Induction	8 (17)	9 (17)
Concomitant to radiation therapy	39 (81)	29 (55)
No. of previous palliative chemotherapy lines, *n* (%)		
0	12 (25)	11 (21)
1	25 (52)	32 (60)
2	11 (23)	10 (19)
Previous platinum-based chemotherapy[a], *n* (%)		
Curative	12 (25)	14 (26)
Palliative	36 (75)	39 (74)
Disease duration (mo)[b]		
Median	19	19
Range	3–156	3–312
Alcohol intake, *n* (%)		
>1 unit/day	31 (65)	31 (59)
<1 unit/day	17 (35)	22 (41)
Smoking status, *n* (%)		
>10 pack-year	32 (67)	31 (58)
<10 pack-year	5 (10)	11 (21)
Unknown	11 (23)	11 (21)

Abbreviation: ECOG, Eastern Cooperative Oncology Group.
[a]Stratification parameter.
[b]Time from first diagnosis to inclusion.