

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Posner MR, Hershock DM, Blajman CR, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *N Engl J Med* 2007;357:1705-15.

Supplementary Table 1. Best Overall Response to Induction Chemotherapy.*

	TPF (N=255)	PF (N=246)
Best overall response — no. (%)		
Complete response	42 (17)	37 (15)
Partial response	141 (55)	121 (49)
No change	30 (12)	41 (17)
Progressive disease	17 (7)	24 (10)
Not evaluable	24 (9)	23 (9)
Missing	1 (0.4)	0
Overall response rate — % (95% confidence interval)	72 (66 to 77)	64 (58 to 70)
P value		0.07
Complete response rate — % (95% confidence interval)	17 (12 to 22)	15 (11 to 20)
P value		0.66

*Defined as the best response recorded from the date of randomization until disease progression or the end of chemotherapy cycles.

Supplementary Table 2. Exposure to Study Drug during Induction Chemotherapy.*

	TPF (N=251)	PF (N=243)
Median no. of cycles	3	3
Median relative dose intensity		
Docetaxel	0.98	—
Cisplatin*	0.99	0.90
5-fluorouracil	0.98	0.88

*Six patients in each group received carboplatin instead of cisplatin.

Abbreviations: PF, cisplatin plus 5-fluorouracil; TPF, docetaxel and cisplatin plus 5-fluorouracil.

Supplementary Table 3. Nonhematologic Adverse Events Regardless of Relationship to Induction Chemotherapy.*

Adverse event	TPF (N=251)		PF (N=243)		P value [†]	
	<i>Percentage of patients</i>					
	All Grades	Grades 3/4	All Grades	Grades 3/4	All Grades	Grades 3/4
Nausea	76	14	80	14	0.39	1.00
Alopecia	68	4	44	1	<0.001	0.09
Stomatitis	66	21	67	27	0.70	0.14
Lethargy	61	5	56	10	0.20	0.03
Vomiting	56	8	63	10	0.17	0.54
Diarrhea	48	7	40	3	0.10	0.07
Anorexia	40	12	34	12	0.16	0.78

Fever in absence of infection	29	4	28	3	0.69	1.00
Constipation	27	1	38	<1	0.01	1.00
Esophagitis/dysphagia/odynophagia	25	13	26	9	0.76	0.26
Infection	23	6	28	5	0.26	0.70
Rash/itch	20	0	16	<1	0.29	0.24
Taste, sense of smell altered	20	<1	17	<1	0.36	0.62
Headache	18	2	15	<1	0.54	0.29
Insomnia	18	<1	17	<1	0.91	1.00
Mood	18	1	18	1	1.00	1.00
Cancer pain	17	9	20	11	0.42	0.45
Edema	17	2	13	1	0.25	1.00
Dizziness	16	4	15	2	0.90	0.17

Gastrointestinal pain/cramping	15	5	10	2	0.17	0.07
Local toxicity	15	<1	15	2	1.00	0.21
Cough	14	<1	15	<1	0.90	1.00
Sensory	14	1	14	<1	0.90	0.62
Weight loss	14	2	14	2	1.00	0.75
Altered hearing	13	1	19	2	0.08	0.33
Heartburn	13	2	13	<1	1.00	0.69
Shortness of breath	12	2	10	2	0.47	1.00
Motor	9	<1	10	2	0.65	0.21

*Adverse events occurring in at least 10% of patients regardless of relationship.

†P values were determined by Fisher's exact test.

Abbreviations: PF, cisplatin plus 5-fluorouracil; TPF, docetaxel and cisplatin plus 5-fluorouracil.

Supplementary Table 4. Adverse Events Regardless of Relationship to Chemoradiotherapy.*

Adverse event	TPF (N=202)		PF (N=184)		P value [†]	
	<i>Percentage of patients</i>					
	All Grades	Grades 3/4	All Grades	Grades 3/4	All Grades	Grades 3/4
Stomatitis	85	37	88	38	0.56	1.00
Esophagitis/dysphagia/odynophagia	68	23	69	24	0.91	0.81
Mouth, nose dryness	57	4	55	4	0.84	1.00
Nausea	43	6	44	6	0.84	1.00
Desquamation	36	4	34	5	0.67	0.63
Rash/itch	34	5	28	2	0.23	0.09
Vomiting	34	3	32	5	0.67	0.46

Weight loss	33	5	38	8	0.34	0.32
Anorexia	32	11	33	15	0.91	0.29
Infection	32	9	33	7	0.83	0.45
Taste, sense of smell altered	32	3	30	4	0.74	0.79
Lethargy	29	6	33	6	0.44	1.00
Constipation	24	<1	30	2	0.21	0.43
Voice changes	21	2	26	2	0.34	1.00
Skin changes	20	3	24	2	0.46	0.75
Sensory	19	<1	15	<1	0.28	1.00
Cough	17	0	17	0	1.00	—
Diarrhea	17	0	20	2	0.51	0.11
Sputum increased	15	4	11	2	0.37	0.14

Cancer pain	14	7	14	9	1.00	0.57
Mood	14	<1	14	2	1.00	0.67
Fever in absence of infection	13	1	19	<1	0.16	0.62
Dizziness	11	2	6	<1	0.10	0.37

*Adverse events occurring in at least 10% of patients regardless of relationship.

†P values were determined by Fisher's exact test.

Abbreviations: PF, cisplatin plus 5-fluorouracil; TPF, docetaxel and cisplatin plus 5-fluorouracil.

Supplementary Table 5. Exposure to Study Treatment During Chemoradiotherapy.

	TPF (N=202)	PF (N=184)
Median dose of radiotherapy — Gy	70	70
Median dose of carboplatin — AUC	9.9*	9.9
Median duration of chemoradiotherapy — wk.	7.1	7.1

*Three patients did not receive carboplatin in the TPF group.

Abbreviations: AUC, area under the curve; PF, cisplatin plus 5-fluorouracil; TPF, docetaxel and cisplatin plus 5-fluorouracil.

Supplementary Figure 1. Study Schema.

Each patient remained in the study and was followed until death or study completion (whichever occurred first), regardless of the number of cycles received.

Response was evaluated by WHO criteria modified by removal of the requirement for confirming a tumor response by a second observation at least 4 weeks after the initial assessment. Since chemoradiotherapy was started as soon as possible after the end of induction chemotherapy, this modification allowed for patients who responded only after the third cycle of induction chemotherapy to proceed to the next phase of treatment without delay.

*Centralized radiation standardization procedures were recommended prior to CRT.

†For patients not evaluable by physical examination.

‡Best response as assessed by the same method used at baseline (CT, MRI).

§Defined as $\geq 25\%$ and $< 50\%$ reduction in tumor size.

¶Defined as $< 25\%$ reduction in tumor size.

Abbreviations: CR, complete response; CRT, chemoradiotherapy; CT, chemotherapy;

CT/MRI, computed tomography/magnetic resonance imaging; NC, no change; PR, partial response.

Supplementary Figure 1.

