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Original article

Platinum rechallenge in recurrent head and neck squamous cell carcinoma after primary chemoradiation

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ABSTRACT

Objective: To evaluate platinum rechallenge efficacy and tolerance in patients presenting recurrent head and neck squamous cell carcinoma (HNSCC) after platinum-based chemoradiation.
Materials and methods: We retrospectively included all patients treated from 2007 to 2016 by platinum-based polychemotherapy for recurrence of HNSCC previously treated by primary or postsurgical platinum-based chemoradiation. The primary end-point was disease control rate (DCR) on platinum rechallenge.
Results: Forty-five patients were included. Median disease-free interval (DFI) after chemoradiation was 5.7 months. DCR on platinum rechallenge was 40%. Progression-free survival at recurrence was 3.7 months and overall survival 5.0 months. DCR in patients with recurrence within 6 months of chemoradiotherapy was 47.8%. DFI > 4.5 months was associated with better DCR: 28.5% versus 54.8%; $P = 0.0311$.
Conclusion: Platinum rechallenge provided good DCR in recurrent HNSCC after chemoradiation.

1. Introduction

Half of patients treated for locally advanced head and neck squamous cell carcinoma (HNSCC) relapse after multimodal treatment [1,2]. The standard treatment for recurrent/metastatic HNSCC is based on the standard EXTREME therapy regimen, associating platinum, 5FU and cetuximab, with median overall survival (OS) of 10.1 months [3]. About 30% of patients treated for recurrent or metastatic HNSCC have already undergone platinum-based treatment [3]. This population has not been specifically studied, despite the fact that their sensitivity to platinum might be lower than the rest of population after the first-line treatment. Moreover, on progression, only nivolumab improves OS; taxane and methotrexate monochemotherapy shows clinical response but no impact on survival [4–6]. Treatment options being limited, clinicians may resort to "rechallenging" platinum-based chemotherapy, especially in patients who showed initial benefit.

Platinum rechallenge has not been studied in HNSCC, but its efficacy is well known in other cancer types, and it is standard practice in ovarian cancer, small-cell pulmonary carcinoma and colorectal cancer in case of relapse more than 6 months after last platinum injection [7–9]. Patients with recurrence within 6 months, on the other hand, are considered platinum-refractory, and alternative treatments are proposed. This attitude is currently under assessment in non-small-cell pulmonary carcinoma [10].

Patients with early recurrence of HNSCC after chemoradiotherapy show median OS <6 months [11], poorer than in case of recurrence later than 6 months. Recent studies suggested that, in recurrence within 6 months, the same treatment may be used as in recurrence after first-line treatment for metastasis [12]. On the hypothesis that patients with early recurrence are platinum-refractory, some teams have proposed a combination of paclitaxel and cetuximab in first line in this situation [13–15]. No studies have compared this attitude versus the EXTREME protocol in early recurrence, although this could lower the number of subsequent chemotherapy lines. In particular, the synergistic effect of cetuximab and platinum would be lost.

Tolerance is a key-point in platinum rechallenge. About 20% of patients present cisplatin-related kidney failure, although this is

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usually reversible [16]. The risk of kidney failure after rechallenge is not known, especially in case of transient creatinine elevation on first-line treatment.

In this context, we aimed to assess the efficacy of platinum rechallenge and tolerance in patients presenting recurrent HNSCC after platinum-based chemoradiotherapy.

2. Methods

2.1. Study design

A single-center retrospective study was performed in François Baclesse Cancer Center, Caen (France). Analyses were based on medical computer records.

The primary endpoint was disease control rate (DCR) on platinum rechallenge. Secondary endpoints were clinical factors associated with progression-free survival (PFS) and overall survival (OS), subsequent treatment lines, and renal tolerance of rechallenge.

2.2. Patients

Inclusion criteria comprised: squamous cell carcinoma of the head and neck treated by platinum-based polychemotherapy, with prior exclusive or postoperative platinum-based chemoradiotherapy, treated between 2007 and 2016; first-line induction chemotherapy was also included. Nasopharyngeal and sinonasal primary tumors were excluded. Patients who underwent primary treatment at another hospital could not be included, due to missing data.

Screening used the local chemotherapy software. In patients treated by the EXTREME protocol, any previous chemoradiation therapy was checked.

2.3. Treatment schedule

The radiation dose was 70 Gy in case of exclusive chemoradiotherapy and ranged between 66 and 70 Gy in postoperative treatment. Initial chemotherapy associated to radiation therapy consisted of: cisplatin 20 mg/m^2/d days 1 to 5, 5fluorouracil (5FU) 1000 mg/m^2/d days 1 to 4 every 3 weeks [17–19], or carboplatin 70 mg/m^2/d + 5FU 600 mg/m^2/d days 1 to 4 every 5 weeks [20,21] followed by cisplatin 100 mg/m^2 every 3 weeks [1].

Chemotherapy for recurrence associated platinum (cisplatin 100 mg/m^2 or carboplatin AUC5), 5FU (4000 mg/m^2 every 3 weeks) and weekly cetuximab (400 mg/m^2 then 250 mg/m^2/week) [3]. Patients treated without 5 FU or with low platinum dose due to comorbidities or poor general health status were also included. Treatment was selected in a multidisciplinary team meeting, but choice of platinum salt was at the discretion of the physician during clinical evaluation.

2.4. Endpoints

Disease control was defined as complete or partial response or stable disease at best response on CT scan using the Response Evaluation Criteria In Solid Tumor v1.1 (RECIST 1.1). Progression or death from any cause was considered as treatment failure. Disease-free interval (DFI) was defined as the time from the last day of chemoradiotherapy to day of first progression. Early recurrence was defined as DFI ≤ 6 months. Progression-free survival 1 (PFS1) was defined as the interval between first day of platinum rechallenge and day of treatment failure after rechallenge, and PFS2 as the interval between first day of second-line treatment and progression or death or end of study (whichever came first). Overall survival (OS) after diagnosis was defined as the interval between initial biopsy to death, and OS after relapse as the interval between first disease on CT and death.

Toxicity was graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Severe comorbidity was defined as a Cumulative Illness Rating Scale item (CIRS) ≥ 3 [22]. Malnutrition was defined as body mass index (BMI) < 18.5 kg/m^2 or weight loss > 10% of body weight [23].

2.5. Statistical analysis

Quantitative variables were reported as median and range, and qualitative variables as number and percentage. PFS and OS with 95% confidence intervals (CI) were estimated following Kaplan–Meier. The log-rank test was used to compare survival. Chi-square or Fisher's exact test was used for categoric variables. Maximum Youden index, calculated as sensitivity + specificity-1, was used to determine optimal cut-off. Analyses used Stata software version 14.0, with two-tailed *P*-values of < 0.05 considered statistically significant.

3. Results

3.1. Patient characteristics at diagnosis and primary treatment

Seventy-four out of 190 patients treated by platinum-based therapy for recurrent/metastatic HNSCC had been previously treated by radiotherapy with concomitant platinum-based chemotherapy, 45 of whom were initially treated at our center.

Table 1 shows patient and tumor characteristics at diagnosis. Median age was 56 years (range, 22–71 years). Thirteen patients had severe comorbidity, but none had more than 1 severe comorbidity. Twenty patients had active nicotine-alcohol co-intoxication. The most frequent primary site was the oral cavity; median stage was IVa.

Table 1
Patient and tumor characteristics at diagnosis.

	n	%
Gender		
Male	40	88.9
Female	5	11.1
Age		
< 65 yr	37	82.2
≥ 65 yr	8	17.8
Smoking		
Active	32	71.1
Past	8	17.8
None	5	11.1
Alcohol abuse		
Active	24	53.3
Past	14	31.1
None	7	15.6
Performance status		
0	17	37.8
1	27	60.0
2	1	2.2
Nutritional status		
Good	29	64.4
Malnutrition	16	35.6
Primary tumor site		
Oral cavity	19	42.2
Oropharynx	13	28.9
Hypopharynx	2	4.4
Larynx	5	11.1
Unknown primary	6	13.3
Stage at diagnosis		
III	3	6.7
IV a	32	71.1
IV b	8	17.8
IV c	2	4.4

Table 2
Primary treatment modalities.

	n	%
Primary surgery	14	31.1
Chemoradiotherapy		
Exclusive	31	68.9
Postoperative	14	31.1
Chemotherapy regimen		
Cisplatin – 5FU	22	48.9
Carboplatin – 5FU	9	20.0
Cisplatin monotherapy	14	31.1
Induction chemotherapy	7	15.6
Radiotherapy technique		
Conformal	26	57.8
IMRT	19	42.2
Radiation dose		
70Gy	41	91.1
66Gy	3	6.7
60Gy	1	2.2

Table 2 shows primary treatments: surgery followed by concomitant chemoradiation with cisplatin for 14 patients; 7 patients received induction chemotherapy (docetaxel, cisplatin, 5FU) before chemoradiotherapy; 22 had exclusive concomitant chemotherapy with cisplatin-5FU and 9 with carboplatin- 5FU.

3.2. Patient characteristics at recurrence

Median DFI was 5.7 months (range, 0.1–45.4 months). Disease progression occurred within 3 months following primary treatment in 5 patients (11.1%), at 3–6 months for 18 (40%), and 6–12 months for 13 (28.9%). Nine patients (20%) had recurrence more than 1 year after primary treatment. Performance status at recurrence was 0–1 for 24 patients (53.3%). Malnutrition was diagnosed at recurrence in 30 cases (66.7%). Progression site was locoregional in16 cases (35.6%), metastatic in 15 (33.3%), and both locoregional and metastatic in 14 (31.1%). A majority of patients with relapse within 6 months after primary treatment showed metastasis ($n = 18/23$: 78.3%). Four of the patients with locoregional progression had salvage surgery and 1 had repeat locoregional radiation therapy ahead of chemotherapy.

3.3. Platinum rechallenge

Therapy regimen at relapse was: cisplatin-5FU-cetuximab ($n = 25$), carboplatin-5FU-cetuximab ($n = 19$), or cisplatin-docetaxel-cetuximab ($n = 1$). Type of platinum administered according to platinum used as primary treatment is detailed in Table 3. Type of platinum in primary treatment was not associated with platinum type used at relapse ($P = 0.264$).

Median number of chemotherapy cycles was 3 (range, 1–6). Eighteen patients completed 4 cycles of chemotherapy or more (40%). Two patients discontinued cetuximab administration due to anaphylactic reaction. Sixteen patients (35.6%) underwent maintenance treatment with cetuximab monotherapy. Median number of maintenance cycles was 4.5 (range, 1–42).

Table 3
Distribution of platinum regimen used at primary treatment and at relapse.

	At primary treatment	
	Cisplatin	Carboplatin
At relapse		
Cisplatin	19	7
Carboplatin	17	2

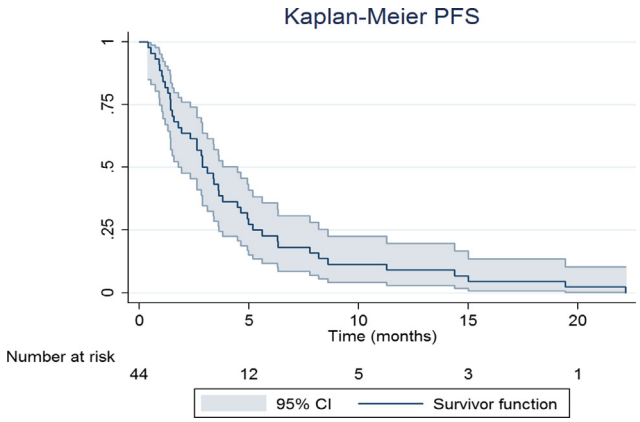

Fig. 1. Progression free survival from relapse (PFS1).

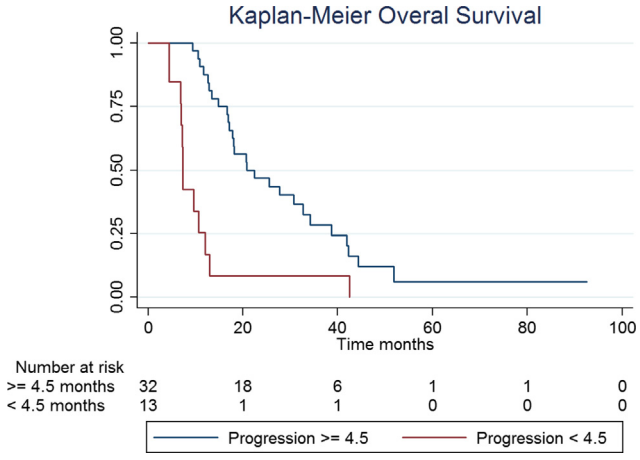

Fig. 2. Overall survival according to 4.5 months disease-free survival cut-off.

3.4. Efficacy of rechallenge

Twenty-one patients (40%) showed disease control with platinum rechallenge: stable disease in 5 (11.1%), partial response in 14 (24.4%) and complete response in 2 (4.4%). No clinical benefit was observed in 24 patients: progressive disease in 13 (28.9%) and death in 11 (24.4%).

Median follow-up after relapse was 17.2 months. Median PFS1 was 3.0 months (range, 2.3–4.6 months) (Figs. 1 and 2); PFS1 was >6 months for 11 patients (24.4%) and > 1 year for 5 patients (11.1%). Maximum treatment response duration was 82 months. Eleven of the 23 patients with early recurrence showed disease control (47.8%).

DFI > 6 months or > 3 months was not significantly associated with better disease control rate (DCR) ($P = 0.555$ and $P = 0.217$ respectively). The DFI cut-off with the best specificity and sensitivity for DCR appeared to be 4.5 months ($P = 0.043$) (28.6% versus 54.8% disease control). Other patient, disease and treatment characteristics were not significantly associated with disease control.

Median OS after initial diagnosis was 17.2 months (range, 12.8–25.5, and 5.0 months (range, 3.7–8.0) after recurrence. There was a significant difference in OS ($P < 0.0001$) using the 4.5 months DFI cut-off: median OS after initial diagnosis was 7.3 (range, 7.0–12.1) and 21.7 months (range, 17.2–32.2) respectively (specificity = 0.42; sensitivity = 0.86; Youden index = 0.27).

Table 4
Second- and third-line chemotherapy.

2nd line		
Total	10	22.2%
Taxane	5	
Immunotherapy	2	
Platinum rechallenge	3	
3rd line		
Total	5	11.1%
Taxane	4	
Immunotherapy	1	

3.5. Renal tolerance at primary treatment

Six of the 36 patients who received concomitant cisplatin as primary treatment (17.7%) presented acute kidney failure during treatment (5 grade 3, 1 grade 2), leading to cancelation of the last cisplatin dose. Only 2 patients (5.6%) presented grade 2 chronic deterioration of glomerular filtration rate.

3.6. Renal tolerance at rechallenge

Nineteen patients received cisplatin treatment at relapse, including 3 who had had transient nephrotoxicity at primary treatment. Two patients had their treatment changed to carboplatin due to grade 3 acute kidney failure at platinum rechallenge, 1 of whom had shown transient nephrotoxicity at primary treatment. Median cumulative cisplatin dose was 600 mg/m^2 (range, 300–1100).

3.7. Second- and third-line chemotherapy after platinum rechallenge

Ten of the 41 patients with progressive disease after platinum rechallenge received second-line systemic treatment (Table 4), with taxanes, immunotherapy (clinical trial), or new platinum rechallenge. Disease control was achieved in 6 patients (60%): stable disease ($n = 3$), or partial response ($n = 3$). Median PFS2 was 3.5 months (range, 1.9–15.6).

One of the 3 patients who had second platinum rechallenge showed complete response to first platinum rechallenge and the other 2 showed partial response. Two presented an objective clinical response to second rechallenge (1 stable disease and 1 partial response, with PFS2 of 3 and 6 months, respectively).

Five patients (11.1%) received third line chemotherapy, with taxanes or immunotherapy. Only 1 presented partial response, with taxane-based treatment.

4. Discussion

Platinum rechallenge in case of recurrent HNSCC after chemoradiotherapy showed a 40% DCR. The usual 6-month DFI cut-off was not associated with poorer outcome: almost half of the patients presenting early recurrence showed benefit from platinum rechallenge. In the present series, a 4.5-month DFI cut-off was significantly associated with better DCR and OS.

In this study, median PFS1 was 3.7 months and median OS at relapse was 5.0 months. Those survival rates are dramatically shorter than in Vermorken's study [3] where PFS and OS were 5.6 and 10.1 months, respectively, and objective response rate (ORR) was 81% using platinum in combination with cetuximab. Many poor prognostic factors were more frequent in our study compared to Vermorken's and can explain the differences in outcome. First, early relapse within 6 months following primary treatment is known to be a major prognostic factor [11], and was an exclusion criterion for Vermorken but not in the present study. Furthermore, oral cavity primary site and metastatic spread are known to be of negative prognosis [24,25] and were more frequent in our study. Retrospective inclusion of non-selected patients also entails more frequent severe comorbidity and malnutrition than in clinical trials, and decreases life expectancy. Another retrospective study [26] with metastatic or recurrent population reported a comparable 48.9% DCR and 11-month median OS; the most frequent primary site was also the oral cavity in their population. Among patients eligible for the EXTREME therapy regimen, those presenting recurrence after chemoradiotherapy are likely a subgroup with poorer prognosis. However, our survival data have to be interpreted with caution due to small sample size and do not allow any specific conclusion to be drawn.

Twenty-two percent of the study population received second-line chemotherapy, which is notably lower than in global metastatic/recurrent HNSCC populations [27]. This might be explained by the poor prognosis of the present population. In case of progression, immunotherapy is the only therapeutic option to have shown a gain in OS, with a median 7.5 months but is not yet available in HNSCC in France. Ferris [12] reported a response rate of 13.3% to nivolumab versus 5.8% to chemotherapy, in second-line treatment or first-line in case of early recurrence after chemoradiotherapy. We found a 47.8% DCR in the early recurrence subgroup, which was dramatically higher than the overall response rate (ORR) in the nivolumab study (subgroup ORR data according to interval to recurrence were not available). Moreover, recent data suggest that immunotherapy could be associated with hyperprogression phenomena in HNSCC, especially in irradiated fields [28]. Thus, in case of early recurrence after chemoradiotherapy, the present study suggests that platinum rechallenge should remain a therapeutic option despite the marketing approval for nivolumab.

Benefit has not been proven for concomitant cisplatin compared to concomitant carboplatin in radiation therapy, although a recent meta-analysis showed a trend for improved outcome [29]. In recurrence, cisplatin showed superiority to carboplatin for overall survival, but no difference in terms of progression-free survival [3]. This is why clinicians prefer to reintroduce cisplatin at relapse, if tolerance was acceptable in primary treatment. Renal toxicity depends on cumulative cisplatin dose, and is more frequent with ≥ 100 mg/m^2. History of hypertension and low serum albumin level are also associated with nephrotoxicity [30]. All these factors are often combined in recurrent HNSCC, which explains why this population is at high risk of kidney failure following cisplatin therapy. Nevertheless, platinum-induced acute kidney failure concerned 5.6% of cases at primary treatment and 10.5% at relapse in our cohort, and moreover is usually transient. Two in 3 patients with kidney failure at primary treatment had cisplatin rechallenge without incurring any nephrotoxicity. This suggests that cisplatin rechallenge can be considered even in case of primary toxicity, if clinical benefit is expected. Prolonged hydration with saline and biological renal function monitoring would help prevent irreversible toxicity [16].

This single-center retrospective study included 45 patients. Statistical analyses did not identify prognostic factors for disease control apart from a 4.5 month DFI cut-off. Due to the small number of patients, a lack of sensitivity cannot be excluded. Furthermore, retrospective recruitment did not include data for certain prognostic factors such as HPV status in oropharyngeal cancers, as P16 status was not systematically assessed at the time of recruitment.

5. Conclusion

Survival in the present population was poorer than in the literature for metastatic or recurrent HNSCC. Nevertheless, disease control was found with platinum rechallenge in 40% of cases, including patients with early recurrence. Optimal disease-free

cut-off for clinical response was 4.5 months. Platinum rechallenge showed acceptable renal tolerance and should continue to play a key role in the therapeutic arsenal for recurrent HNSCC despite the advent of immunotherapies.

Ethical considerations

Review-board approval was not required for this single-center retrospective study. At first consultation, patients received explicit information indicating that their data could be used for research purposes. None expressed opposition.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Bernier J, Domenge C. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004:1945–52.
[2] Adelstein DJ, Li Y, Adams GL, Wagner H, Kish JA, Ensley JF, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol 2003;21(1):92–8.
[3] Vermorken JB, Mesia R, Rivera F, Remenar E, Kawecki A, Rottey S, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. N Engl J Med 2008;359(11):1116–27.
[4] Catimel G, Verweij J, Mattijssen V, Hanauske A, Piccart M, Wanders J, et al. Docetaxel (Taxotere®): An active drug for the treatment of patients with advanced squamous cell carcinoma of the head and neck. Ann Oncol 1994;5(6):533–7 [Oxford University Press].
[5] Forastiere AA, Shank D, Neuberg D, Taylor SG, DeConti RC, Adams G. Final report of a phase II evaluation of paclitaxel in patients with advanced squamous cell carcinoma of the head and neck. Cancer 1998;82(11):2270–4 [John Wiley & Sons, Inc.].
[6] Capizzi RL, DeConti RC, Marsh JC, Bertino JR. Methotrexate therapy of head and neck cancer: improvement in therapeutic index by the use of leucovorin "Rescue". Cancer Res 1970;30(6):1782–8 [American Association for Cancer Research].
[7] Ledermann J, Colombo N, du Bois a, Torri V, Floriani I, Qian W, et al. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial 2003;361:2099–106.
[8] Genestreti G, Metro G, Kenmotsu H, Wakuda K, Battista M Di, Cavallo G, et al. Final outcome results of platinum-sensitive small cell lung cancer (SCLC) patients treated with platinum-based chemotherapy rechallenge: a multi-institutional retrospective analysis 2014:12–3.
[9] Chibaudel B, Tournigand C, Bonnetain F, Maindrault-Goebel F, Lledo G, André T, et al. Platinum-sensitivity in metastatic colorectal cancer: towards a definition. Eur J Cancer 2013;49(18):3813–20 [Pergamon].
[10] Bluthgen MV, Besse B. Second-line combination therapies in nonsmall cell lung cancer without known driver mutations. Eur Respir Rev 2015;24(138):582–93.
[11] Saloura V, Cohen EEW, Licitra L, Billan S, Dinis J, Lisby S, et al. An open-label single-arm, phase II trial of zalutumumab, a human monoclonal anti-EGFR antibody, in patients with platinum-refractory squamous cell carcinoma of the head and neck. Cancer Chemother Pharmacol 2014;73(6):1227–39 [Springer Berlin Heidelberg].
[12] Ferris RL, Blumenschein G, Fayette J, Guigay J, Colevas AD, Licitra L, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. N Engl J Med 2016 [NEJMoa1602252].
[13] Fayette J, Montella A, Bachelot T, Pommier P, Girodet D, Racadot S, et al. Paclitaxel in relapsed squamous cell carcinoma of head and neck (SSCHN): retrospective study of a single institution. J Clin Oncol 2009:e17047.
[14] Péron J, Ceruse P, Lavergne E, Buiret G, Pham B-N, Chabaud S, et al. Paclitaxel and cetuximab combination efficiency after the failure of a platinum-based chemotherapy in recurrent/metastatic head and neck squamous cell carcinoma. Anticancer Drugs 2012:1.
[15] Bernad IP, Trufero JM, Urquizu LC, Pazo Cid RA, de Miguel AC, Agustin MJ, et al. Activity of weekly paclitaxel–cetuximab chemotherapy in unselected patients with recurrent/metastatic head and neck squamous cell carcinoma: prognostic factors. Clin Transl Oncol 2017;19(6):769–76 [Springer International Publishing].
[16] Yao X, Panichpisal K, Kurtzman N, Nugent K. Cisplatin nephrotoxicity: a review. Am J Med Sci 2007;334(2):115–24.
[17] Pignon J-P, le Maître A, Maillard E, Bourhis J, MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. Radiother Oncol 2009;92(1):4–14.
[18] Taylor SG, Murthy AK, Showel JL, Caldarelli DD, Hutchinson JC, Holinger LD, et al. Improved control in advanced head and neck cancer with simultaneous radiation and cisplatin/5-FU chemotherapy. Cancer Treat Rep 1985;69(9):933–9.
[19] Taylor SG, Murthy AK, Griem KL, Recine DC, Kiel K, Blendowski C, et al. Concomitant cisplatin/5-FU infusion and radiotherapy in advanced head and neck cancer: 8-year analysis of results. Head Neck 1997;19(8):684–91 [Wiley Subscription Services, Inc., A Wiley Company].
[20] Calais G, Alfonsi M, Bardet E, Sire C, Germain T, Bergerot P, et al. Randomized trial of radiation therapy versus concomitant chemotherapy and radiation therapy for advanced-stage oropharynx carcinoma. J Natl Cancer Inst 1999;61(24):2081–6.
[21] Denis F, Garaud P, Bardet E, Alfonsi M, Sire C, Germain T, et al. Final results of the 94-01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant chemoradiation in advanced-stage oropharynx carcinoma. J Clin Oncol 2004;22(1):69–76.
[22] Linn BS, Linn MW, Gurel L. Cumulative Illness Rating Scale. J Am Geriatr Soc 1968;16(5):622–6.
[23] Évaluation diagnostique de la dénutrition protéino-énergétique des adultes hospitalisés. ANAES Serv des recommandations Prof.; 2003.
[24] Leeman JE, Li J, Pei X, Venigalla P, Zumsteg ZS, Katsoulakis E, et al. Patterns of treatment failure and postrecurrence outcomes among patients with locally advanced head and neck squamous cell carcinoma after chemoradiotherapy using modern radiation techniques. JAMA Oncol 2017;3(11):1487 [American Medical Association].
[25] Argiris A, Li Y, Forastiere A. Prognostic factors and long-term survivorship in patients with recurrent or metastatic carcinoma of the head and neck. Cancer 2004;101(10):2222–9.
[26] De Mello RA, Geros S, Alves MP, Moreira F, Avezedo I, Dinis J. Cetuximab plus platinum-based chemotherapy in head and neck squamous cell carcinoma: a retrospective study in a single comprehensive European cancer institution. PLoS One 2014;9(2):1–7.
[27] Siano M, Infante G, Resteghini C, Cau MC, Alfieri S, Bergamini C, et al. Outcome of recurrent and metastatic head and neck squamous cell cancer patients after first line platinum and cetuximab therapy. Oral Oncol 2017;69:33–7 [Elsevier Ltd].
[28] Saâda-Bouzid E, Defaucheux C, Karabajakian A, Coloma VP, Servois V, Paoletti X, et al. Hyperprogression during anti-PD-1/PD-L1 therapy in patients with recurrent and/or metastatic head and neck squamous cell carcinoma. Ann Oncol 2017;28(7):1605–11.
[29] Aguiar PN, Tadokoro H, Da Silva GF, Landgraf MM, Noia Barreto CM, Filardi BA, et al. Definitive chemoradiotherapy for squamous head and neck cancer: Cisplatin versus carboplatin? A meta-analysis. Futur Oncol 2016;12(23):2755–64.
[30] Motwani SS, McMahon GM, Humphreys BD, Partridge AH, Waikar SS, Curhan GC. Development and validation of a risk prediction model for acute kidney injury after the first course of Cisplatin. J Clin Oncol 2018 [JCO2017757161].