Comparison for first curative treatment for localized or locally advanced head and neck squamous cell carcinomas (L(A)-HNSCC) between exclusive (chemo)radiation and surgery or induction chemotherapy: sub-analysis of the EPOCKS study.

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Abstract

BACKGROUND :

The initial curative standard therapy for LAHNSCC by exclusive CRT (chemoradiotherapy) or surgery (+/- CRT) have similar results in term of PFS and OS. Indication depends on several factors including regional expertises and anticipated sequela. The role of induction chemotherapy (IC) remains questionable until today. Previous publications suggested that surgery followed by CRT could be relevant for high-risk relapse tumors. The aim of this retrospective study was to compare as first-intent curative treatment (C)RT to alternative approach (S/IC: surgery and/or IC +/- CRT).

METHODS :

1120 patients (pts) with a LAHNSCC treated for the first time in 1998, 2004 or 2006 were retrospectively analyzed and 977 were finally evaluable. Pts were distributed according to their first curative treatment: (C)RT or S/IC. Overall (OS) and progression-free survival (PFS) were compared using Kaplan-Meier analyses. OS and PFS are calculated from the start date of treatment.

RESULTS :

With a median follow-up of 3.3 years (95% IC 3.0-3.6), 335 pts died and the median PFS were 4.0 years in the whole population. A statistically significant lower PFS (HR = 1.26; CI95% [1.01-1.59]; p=0.0439) and lower OS (HR = 1.50; CI95% [1.16-1.95]; p=0.0023) were observed with CRT group compared to S/IC group (adjusted for the variables stage T, Stage N and age at diagnosis). Weekly and tri-weekly cisplatin received as potentiation of RT were also explored for the 200 receiving platin. No difference in PFS or OS were observed but statistical power is weak.

CONCLUSIONS :

This large retrospective study suggests that the standard (C)RT for LASCCHN could be optimize by adding initial surgery or/and IC. Randomized trials are warranted to conclude.

Study overview

Repeated cross-sectional study with retrospective data collection carried out as part of the EPOCKS study on practice analyzes by center.

Main objective

1) difference in terms of OS and PFS of a first-intent curative treatment with chemoradiotherapy (CRT) compared to a treatment not including an exclusive CRT (surgery, induction chemotherapy)
2) non-inferiority of weekly cisplatin versus cisplatin every 3 weeks in terms of chemotherapy treatment concomitant with curative radiotherapy

Inclusion criteria

- new files in 1998, 2004 or 2006
- localized or locally advanced stage of a squamous cell carcinoma of the oral cavity, oropharynx, larynx or hypopharynx

Exclusion criteria

- association with another cancer
- previous irradiation of the upper aerodigestive tract
- patients whose treatment would not be covered in the regions studied

Baseline characteristics

All patients with squamous cell carcinoma treated as initial treatment in 1998, 2004 or 2006 in selected structures in Rhône-Alpes and Doubs.

	(C)RT Exclusive RCT or exclusive RT N=238	S/IC surgery and/or induction chemotherapy +/- (C)RT N=739
Median age	62.6 (38.0 - 90.8)	58.6 (21.6 - 91.7)
Stage		
Missing data	15	16
I-II	67 (30%)	254 (35%)
III	49 (22%)	183 (25%)
IV	107 (48%)	286 (40%)
Location		
Missing data	15	4
Oral Cavity	18 (8.1%)	145 (19.7%)
Larynx	54 (24.2%)	242 (32.9%)
Oropharyngeal	93 (41.7%)	245 (33.3%)
Hypopharyngeal	58 (26.0%)	103 (14.0%)
IC		
No	238 (100.0%)	521 (70.5%)
Yes	0 (0.0%)	218 (29.5%)
Surgery of the primary tumor		
No	238 (100.0%)	151 (20.4%)
Yes	0 (0.0%)	588 (79.6%)
RT		(after IC or surgery)
No	0 (0.0%)	239 (32.3%)
Yes	238 (100%)	500 (67.7%)
Potentiation of RT		
Yes		346 (35.4%)
Whom cisplatin		200
Weekly		76 (38.0%)
Tri-Weekly		124 (62.0%)

Table 1 : Characteristics of the 977 patients according to the exclusive (C)RT or non-exclusive (C)RT group.

The initial population included 1120 patients including 661 with a living status and 372 with a deceased status but the analysis population therefore consisted of 977 patients due to missing data.

The median age at the initiation of treatment (radiotherapy, chemotherapy or surgery) was 59.3 years. 218 patients (22.3%) received neoadjuvant chemotherapy and 588 (60.2%) surgeries. Regarding radiotherapy, 257 patients (26.3%) benefited from postoperative radiotherapy, 89 (9.1%) from exclusive radiotherapy and 346 (46.9%) from radiotherapy potentiated by chemotherapy. It should be noted that the patients had no proven metastases at the time of diagnosis.

OS Results

The analyzes included 977 patients. Median duration of follow-up was 3.3 years 95% CI [3.0; 3.6]. Interpretation of the curves after 3 years was therefore limited. For this reason, the medians of survival are not given. We found a **statistically significant difference in overall survival** in favor of group 2 with a HR of 1.41 [95% CI 1.11-1.79] (p = 0.0053) (Figure 1). The 3-year overall survival rates were 68.1% in group 2 [95% CI 64.1-71.7%] versus 59.2% in group 1 [95% CI 51.4-66.2%]. The difference between the two groups remains significant with a HR = 1.50 [95% CI 1.16-1.95] (p = 0.0023) once adjusted for the variables stage T, Stage N and age at diagnosis.

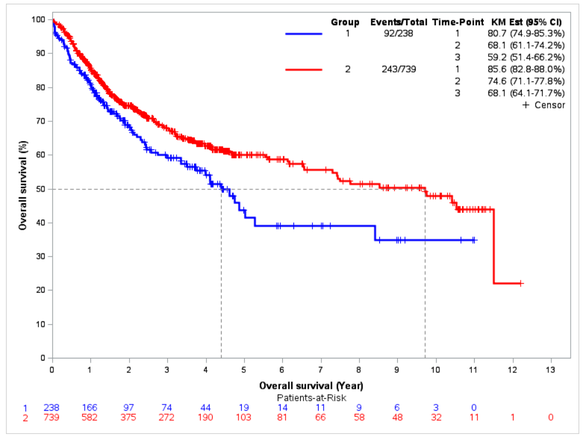

Figure 1 : Overall survival curves by Kaplan Meier according to treatment group (Group 1: Exclusive CRT or exclusive RT ; Group 2 : surgery and/or induction chemotherapy +/- CRT)

PFS Results

Regarding progression-free survival, 461 patients died or progressed out of the 974 patients who could be analyzed (Supplementary figure 2). We found a **statistically significant difference in progression-free survival** in favor of group 2 with a HR of 1.25 [95% CI 1.01-1.54] (P-value at 0.0394). The 3-year progression-free survival rates were 55.6 % in group 2 [95% CI 51.6-59.4 %] versus 52.0 % in group 1 [95% CI 44.9-58.7 %]. The difference between the two groups remains significant with a HR = 1.26 [95% CI 1.01-1.59] (p = 0. 0439) once adjusted for the variables stage T, Stage N and age at diagnosis.

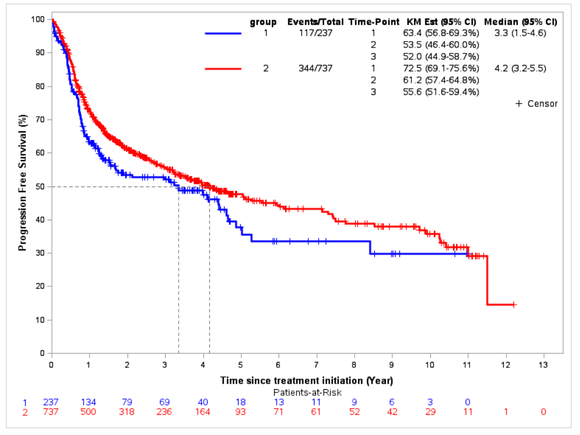

Figure 2 : Kaplan Meier progression-free survival curves by treatment group (Group 1 : Exclusive CRT or exclusive RT ; Group 2 : surgery and/or induction chemotherapy +/- CRT)

Concomitant chemotherapy analyzes

The radio-chemotherapy-treated subgroup included 346 patients, with weekly cisplatin for 76 patients, cisplatin every 3 weeks for 124 patients and another chemotherapy for 146 patients. There was no significant difference between the weekly cisplatin and every 3 weeks cisplatin groups, either in terms of progression-free survival with a HR of 0.92 [95% CI 0.61-1.38; p-value = 0.6787] (Supplementary figure 3 and table 3). There was also no significant difference in terms of overall survival with a HR of 0.70 [95% CI 0.42-1.17; p-value = 0.1714].

Conclusions

In conclusion, our study made it possible to show that in our patients, presenting a localized or locally advanced squamous cell carcinoma of the head and neck, the initial treatment by radiotherapy or exclusive radio-chemotherapy was inferior in terms of overall survival or progression-free survival, compared to treatment without radiotherapy or exclusive radio-chemotherapy. In addition, weekly cisplatin did not appear to be inferior to cisplatin every three weeks in terms of OS and PFS under concomitant treatment with radiotherapy, but statistical power is weak.

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