

# **Comparaison des toxicités aiguës de la Radiothérapie ORL entre fumeurs et non- fumeurs : une étude prospective monocentrique.**

Camille Invernizzi, 24 Novembre 2023



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**Absence de lien d'intérêt.**

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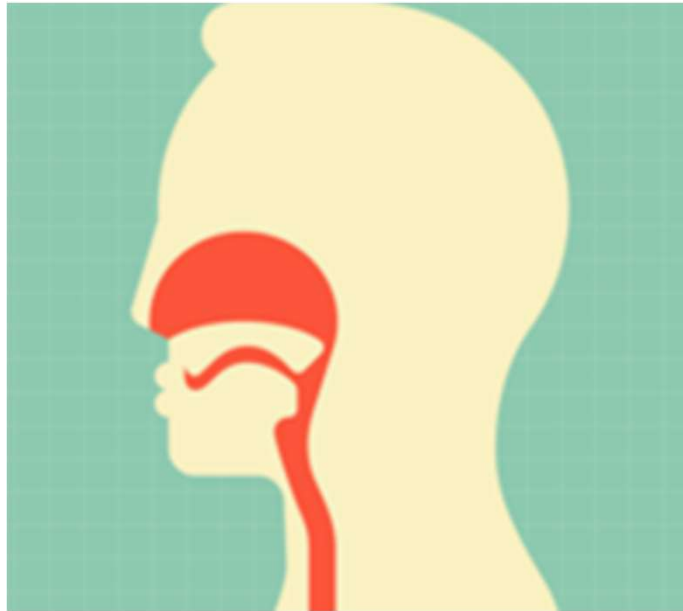
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# Cancers ORL



Source : Institut National du Cancer

# Epidémiologie

**890 000**

*Nouveaux cas par an de  
**cancers ORL** dans le monde*

**507 000 décès**

**8 Millions**

*Décès par an dûs au **tabac**  
dans le monde*

**1<sup>ère</sup> cause de décès  
évitables**

# Indications de traitement

**Stades I-II**  
cT1-T2 N0



- ✓ Chirurgie
- ✓ Radiothérapie +/- CT

**Stades III-IV**  
cT3-T4 et/ou N+



- ✓ Chirurgie puis (chimio)radiothérapie
- ✓ Radio-chimiothérapie (RTCT)

# Facteurs influençant les toxicités de la RT ORL



**Toxicités de la  
Radiothérapie  
ORL**

**Aigües : <3-6 mois**  
**Tardives : >6 mois**

# Facteurs influençant les toxicités de la RT ORL

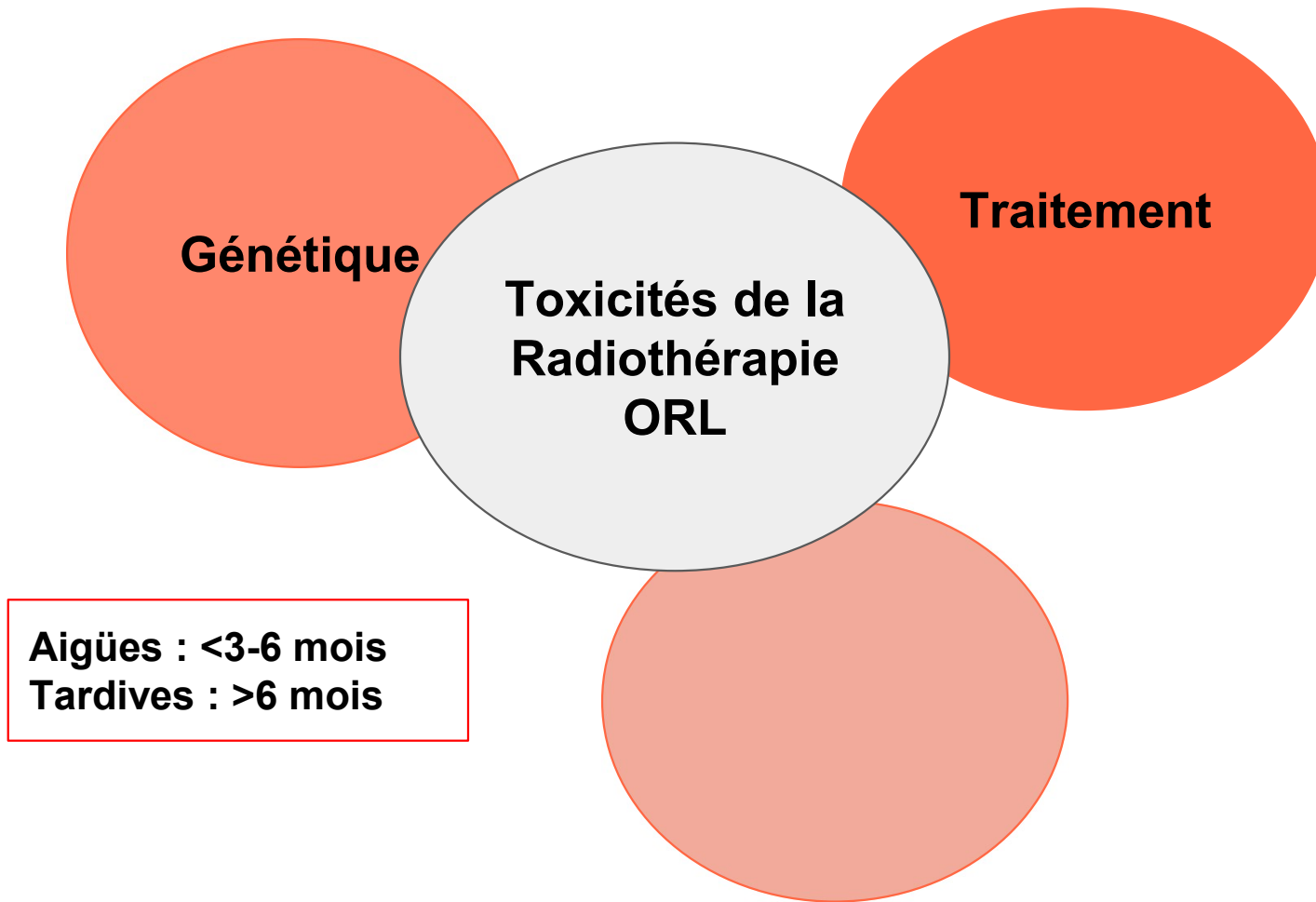
**Génétique**

**Toxicités de la  
Radiothérapie  
ORL**

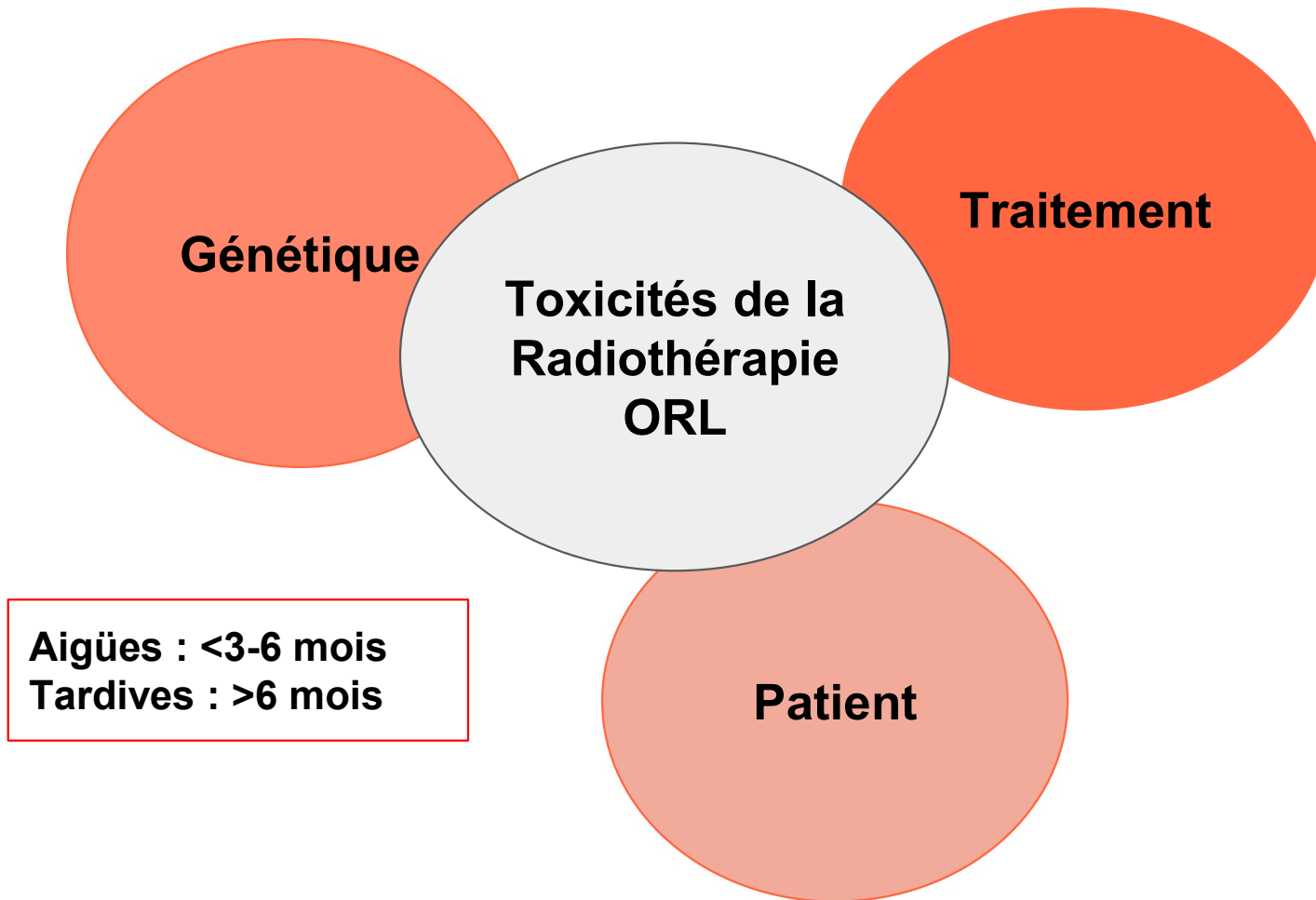
**Aigües : <3-6 mois  
Tardives : >6 mois**



# Facteurs influençant les toxicités de la RT ORL

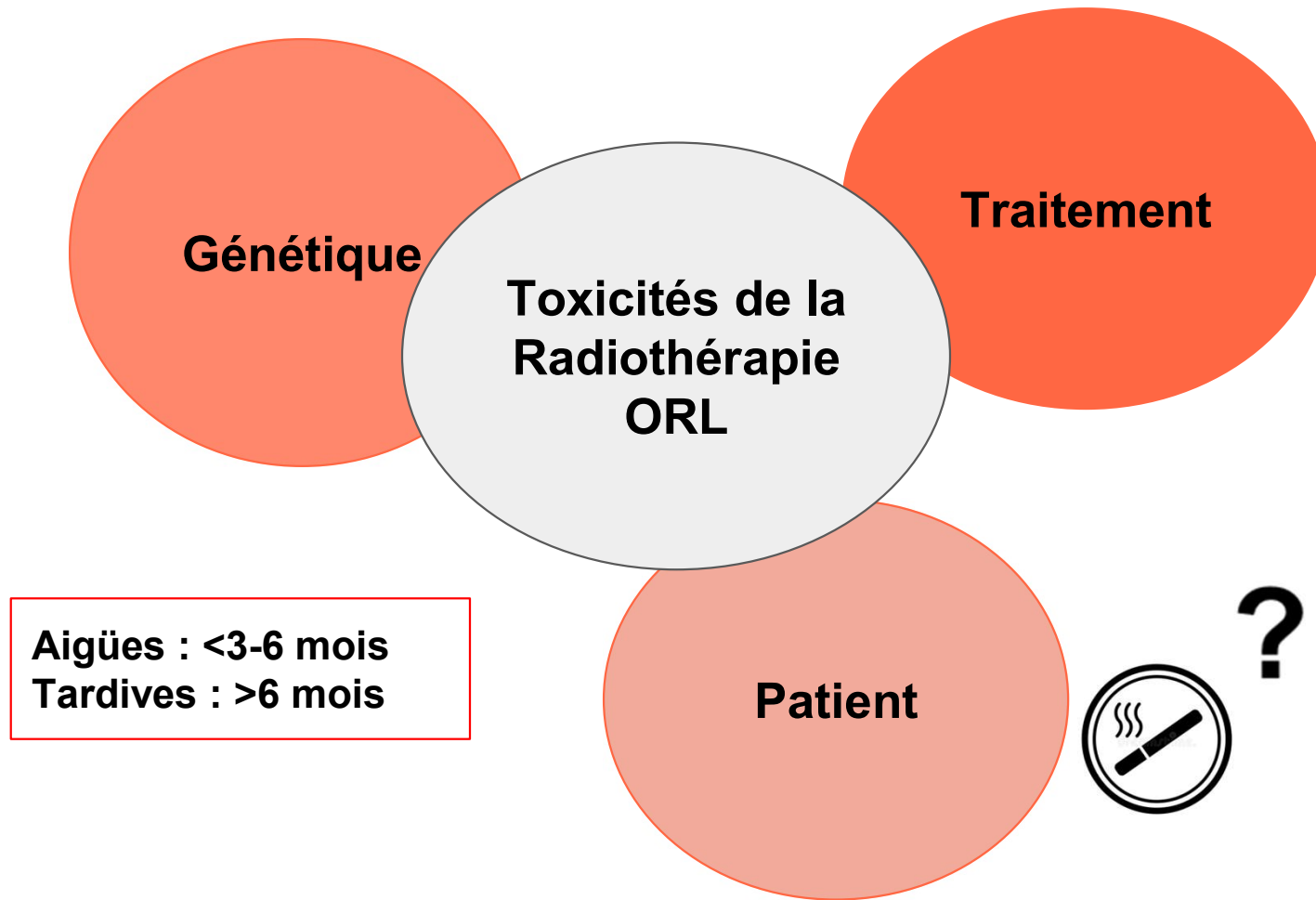


# Facteurs influençant les toxicités de la RT ORL



**Aigües : <3-6 mois**  
**Tardives : >6 mois**

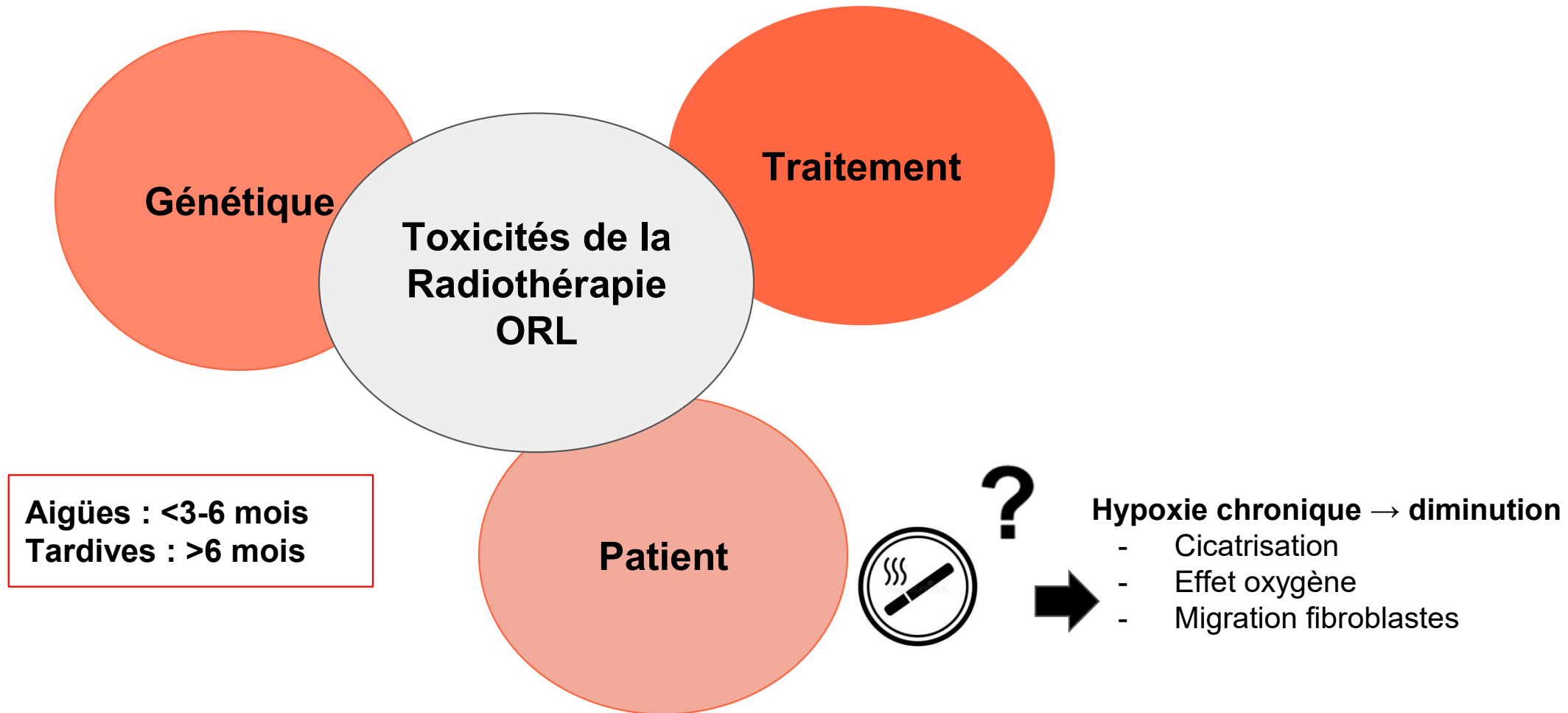
# Facteurs influençant les toxicités de la RT ORL



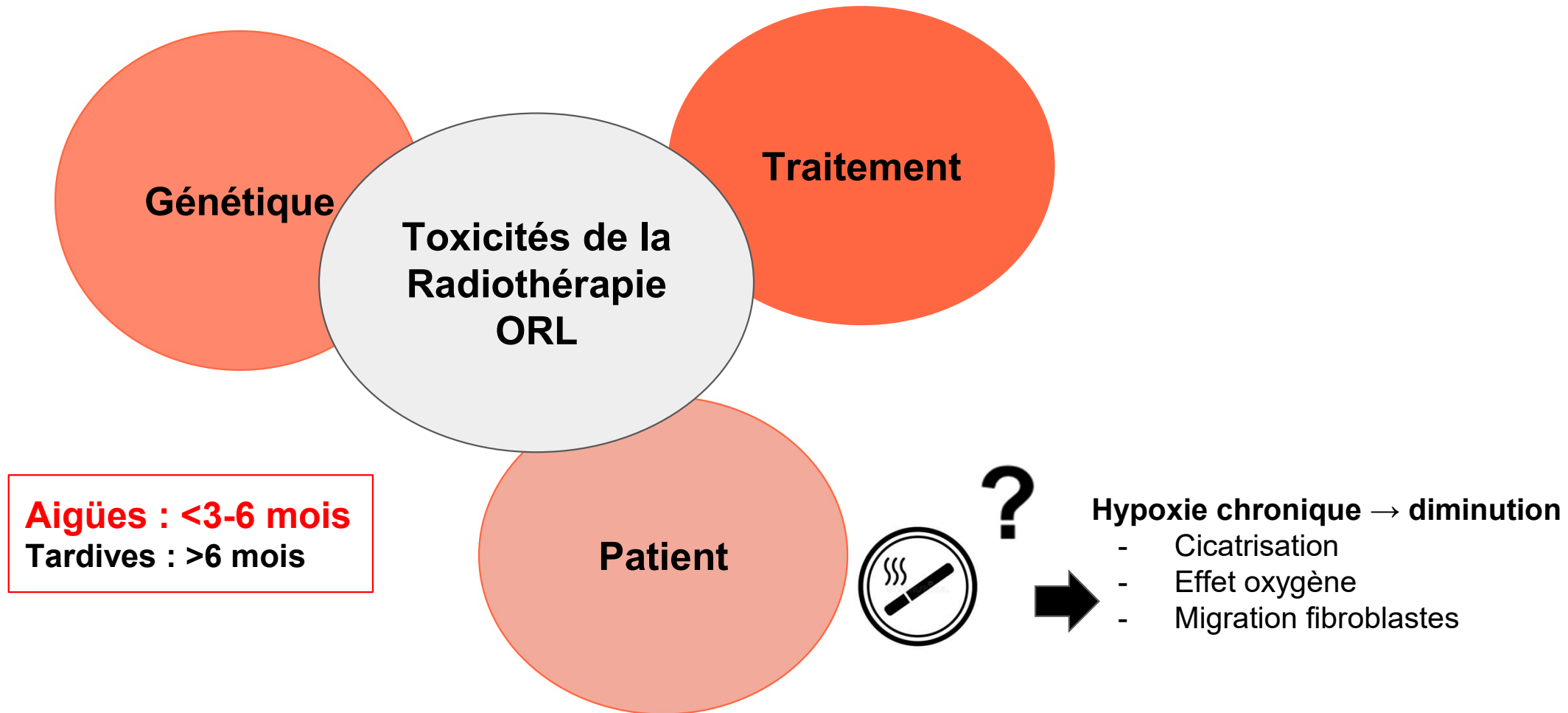
**Aigües : <3-6 mois**  
**Tardives : >6 mois**



# Facteurs influençant les toxicités de la RT ORL



# Facteurs influençant les toxicités de la RT ORL



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# Tabagisme et toxicités aiguës radio-induites



de dermatites

# Tabagisme et toxicités aiguës radio-induites



de dermites



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# Objectifs



# Objectifs de l'étude

- ❑ **Objectif principal** : Étudier l'association entre le **tabagisme actif** et la survenue d'au moins une **toxicité aiguë** (mucite et/ou dermite et/ou dysphagie) de grade 3-4 du CTCAE v.5.0

# Objectifs de l'étude

- ❑ **Objectif principal** : Étudier l'association entre le **tabagisme actif** et la survenue d'au moins une **toxicité aiguë** (mucite et/ou dermite et/ou dysphagie) de grade 3-4 du CTCAE v.5.0
  
- ❑ **Objectifs secondaires** :
  - ❑ Étudier l'association entre le **tabagisme actif** et la survenue d'une **mucite**, d'une **dermite** et d'une **dysphagie aiguës** de grade 3-4 du CTCAE v.5.0

# Objectifs de l'étude

- ❑ **Objectif principal** : Étudier l'association entre le **tabagisme actif** et la survenue d'au moins une **toxicité aiguë** (mucite et/ou dermite et/ou dysphagie) de grade 3-4 du CTCAE v.5.0
  
- ❑ **Objectifs secondaires** :
  - ❑ Étudier l'association entre le **tabagisme actif** et la survenue d'une **mucite**, d'une **dermite** et d'une **dysphagie aiguës** de grade 3-4 du CTCAE v.5.0
  - ❑ Rechercher d'**autres facteurs associés** à la survenues de toxicités aiguës de grade 3-4 du CTCAE v.5.0

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# Matériels et Méthodes

# Population

## ❑ Critères d'inclusion

- Indication de Radiothérapie pour un cancer ORL
- Dose  $\geq$  66 Gy

## ❑ Critères d'exclusion

- Traitement antérieur de Radiothérapie ORL

# Données recueillies

- ❑ **Patient** : âge, Performans Status, IMC, statut tabagique, OH, dénutrition, diabète, prise de Metformine
- ❑ **Tumeur** : cTNM, pTNM, histologie, stade, localisation, p16, marges de résection
- ❑ **Traitement** : type (chirurgie, CT, RTCT), nombre de cycles de CT, curage, dose totale, étalement, technique, suspension et arrêt des traitements, hospitalisation, V20 et V30 cavité buccale

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# Déroulement d'une inclusion

Consultation  
d'annonce



Scanner de  
centrage

Début du  
traitement

Évaluations  
hebdomadaires



Fin du  
traitement

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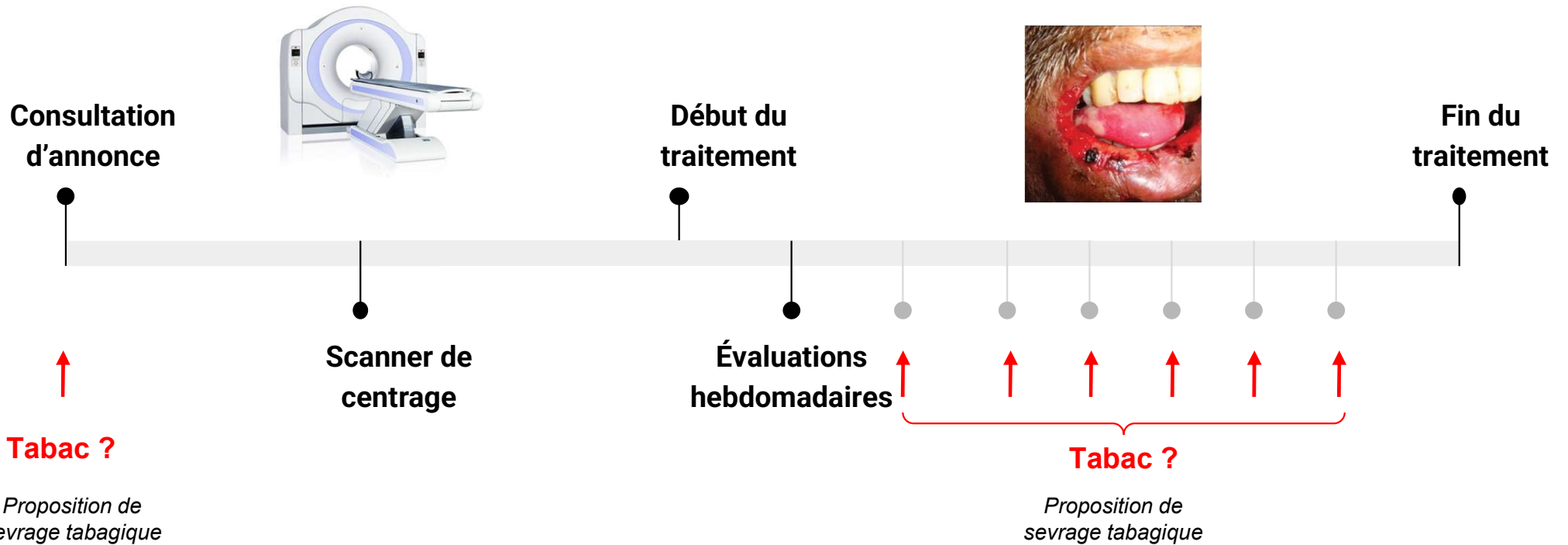
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# Déroulement d'une inclusion





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# Statut tabagique

✓ Fumeurs actifs

✓ Anciens fumeurs sevrés  
✓ N'ayant jamais fumé

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# Statut tabagique

## Fumeurs actifs

✓ Fumeurs actifs

## Non-Fumeurs

✓ Anciens fumeurs sevrés  
✓ N'ayant jamais fumé

# Statut tabagique

## Fumeurs actifs

✓ Fumeurs actifs

- + reprise du tabac
- + arrêt du tabac en cours de RT

## Non-Fumeurs

- ✓ Anciens fumeurs sevrés
- ✓ N'ayant jamais fumé

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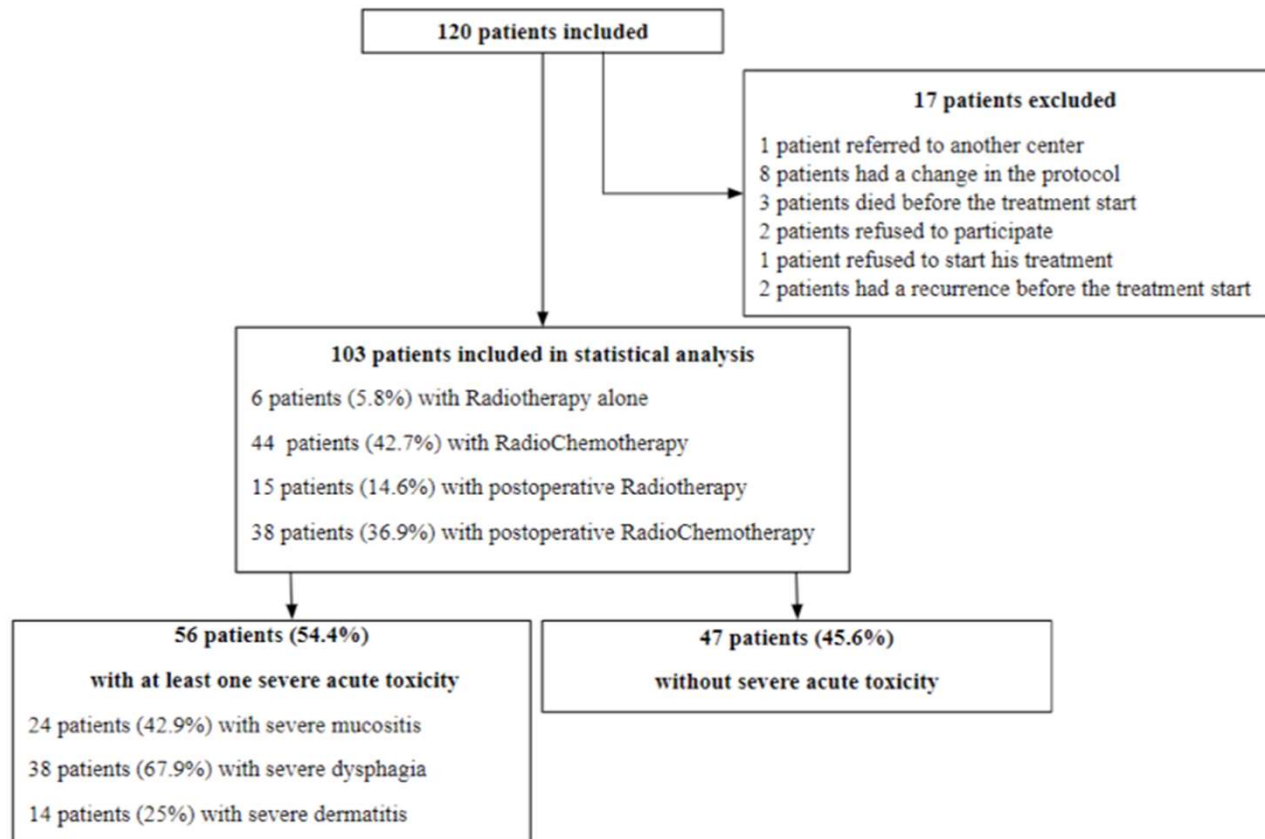
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# Résultats

# Flow chart de l'étude



**Figure 1.** Flow chart of the study

# Population

**Table 1.** Baseline characteristics of patients, pathological features and treatments

	N(%) unless otherwise indicated		
<b>Age, means±SD, years</b>	63.0±8.9	<b>Cancer localization</b>	
<b>BMI, means±SD, kg/m<sup>2</sup></b>	24.5±5.3	Oropharynx	32 (31.1)
<b>Malnutrition<sup>1</sup></b>	15 (14.6)	Larynx	18 (17.5)
<b>Sex</b>		Oral cavity	31 (30.1)
Women	27 (26.2)	Hypopharynx	15 (14.6)
Men	76 (73.8)	Others <sup>2</sup>	7 (6.8)
<b>Performance status</b>		<b>Type of treatment</b>	
0	33 (32.0)	Radiotherapy alone	6 (5.8)
1	60 (58.3)	Radiochemotherapy	44 (42.7)
2	9 (8.7)	Postoperative radiotherapy	15 (14.6)
3	1 (1.0)	Postoperative radiochemotherapy	38 (36.9)
4	0 (0.0)	<b>Surgery</b>	53 (51.5)
<b>Smoking status</b>		Type of resection	
Never smokers	14 (13.6)	R0	25 (47.2)
Former smokers	60 (58.2)	R1	25 (47.2)
Active smokers	29 (28.2)	R2	3 (5.6)
Number of pack-years, median [IQR]	40 [35-50]	<b>Systemic therapy</b>	
Number of cigarettes/day, median [IQR]	6 [3-10]	Chemotherapy	72 (69.9)
<b>Alcohol status</b>		Cisplatin 100 mg/m <sup>2</sup>	66 (91.7)
Never drinkers	38 (36.9)	Number of CDDP	
Former drinkers	29 (28.2)	1	6 (9.2)
Current drinkers	36 (34.9)	2	29 (44.6)
<b>Diabetes</b>	14 (13.6)	3	30 (46.1)
Metformin taking	12 (11.7)	Cisplatin 40 mg/m <sup>2</sup>	3 (4.2)
<b>cT</b>		Carboplatin AUC 2	1 (1.4)
T1	10 (9.7)	Carboplatin AUC 5	2 (2.8)
T2	23 (22.3)	Cetuximab	10 (9.7)
T3	28 (27.2)	<b>Radiotherapy</b>	
T4	37 (35.9)	Overall duration of radiotherapy, means±SD, days	48±7
Tx	5 (4.9)	<b>Total dose</b>	
<b>cN</b>		70 Gy	57 (55.3)
N0	40 (38.8)	66 Gy	46 (44.7)
N1	8 (7.8)	<b>Fractionation schedule</b>	
N2	46 (44.7)	2.12 Gy by fraction	56 (54.4)
N3	8 (7.8)	2 Gy by fraction	47 (45.6)
Nx	1 (1.0)	<b>Total suspension of radiotherapy</b>	24 (23.3)
<b>pT<sup>2</sup></b>		Number of days of suspension, median [IQR]	3 [3-5]
T1	3 (5.7)	<b>Technique of radiotherapy</b>	
T2	15 (28.3)	Tomotherapy	84 (81.6)
T3	19 (35.8)	VMAT	19 (18.4)
T4	14 (26.4)	<b>OAR doses</b>	
Tx	2 (3.8)	V20 oral cavity, means±SD, %	83.2±22.5
<b>pN<sup>2</sup></b>		V30 oral cavity, means±SD, %	68.0±30.7
0	17 (32.1)		
1	9 (17.0)		
2	13 (24.5)		
3	12 (22.6)		
Nx	2 (3.8)		
<b>Stage</b>			
I/II	27 (26.2)		
III/IV	76 (73.8)		
<b>HPV status<sup>3</sup></b>			
Positive	14/32 (43.7)		
Negative	18/32 (56.3)		

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<b>Sex</b>			
Women	27 (26.2)		
Men	76 (73.8)		
<b>Performance status</b>			
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<b>Smoking status</b>			
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<b>cT</b>			
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Positive	14/32 (43.7)		
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<b>Cancer localization</b>			
Oropharynx		32 (31.1)	
Larynx		18 (17.5)	
Oral cavity		31 (30.1)	
Hypopharynx		15 (14.6)	
Others <sup>4</sup>		7 (6.8)	
<b>Type of treatment</b>			
Radiotherapy alone		6 (5.8)	
Radiochemotherapy		44 (42.7)	
Postoperative radiotherapy		15 (14.6)	
Postoperative radiochemotherapy		38 (36.9)	
<b>Surgery</b>		53 (51.5)	
Type of resection			
R0		25 (47.2)	
R1		25 (47.2)	
R2		3 (5.6)	
<b>Systemic therapy</b>			
Chemotherapy		72 (69.9)	
Cisplatin 100 mg/m <sup>2</sup>		66 (91.7)	
Number of CDDP			
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2		29 (44.6)	
3		30 (46.1)	
Cisplatin 40 mg/m <sup>2</sup>		3 (4.2)	
Carboplatin AUC 2		1 (1.4)	
Carboplatin AUC 5		2 (2.8)	
Cetuximab		10 (9.7)	
<b>Radiotherapy</b>			
Overall duration of radiotherapy, means±SD, days		48±7	
Total dose			
70 Gy		57 (55.3)	
66 Gy		46 (44.7)	
Fractionation schedule			
2.12 Gy by fraction		56 (54.4)	
2 Gy by fraction		47 (45.6)	
Total suspension of radiotherapy		24 (23.3)	
Number of days of suspension, median [IQR]		3 [3-5]	
Technique of radiotherapy			
Tomotherapy		84 (81.6)	
VMAT		19 (18.4)	
<b>OAR doses</b>			
V20 oral cavity, means±SD, %		83.2±22.5	
V30 oral cavity, means±SD, %		68.0±30.7	

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T1	3 (5.7)		
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T3	19 (35.8)		
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<b>pN<sup>2</sup></b>			
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## Cancer localization

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## Type of resection

R0	25 (47.2)
R1	25 (47.2)
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## Systemic therapy

<b>Chemotherapy</b>	72 (69.9)
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Cetuximab	10 (9.7)

## Radiotherapy

<b>Overall duration of radiotherapy, means±SD, days</b>	48±7
<b>Total dose</b>	
70 Gy	57 (55.3)
66 Gy	46 (44.7)

## Fractionation schedule

2.12 Gy by fraction	56 (54.4)
2 Gy by fraction	47 (45.6)

## Total suspension of radiotherapy

Number of days of suspension, median [IQR]	24 (23.3)
--	-----------

## Technique of radiotherapy

Tomotherapy	84 (81.6)
VMAT	19 (18.4)

## OAR doses

V20 oral cavity, means±SD, %	83.2±22.5
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T4	37 (35.9)
Tx	5 (4.9)
<b>cN</b>	
N0	40 (38.8)
N1	8 (7.8)
N2	46 (44.7)
N3	8 (7.8)
Nx	1 (1.0)
<b>pT<sup>2</sup></b>	
T1	3 (5.7)
T2	15 (28.3)
T3	19 (35.8)
T4	14 (26.4)
Tx	2 (3.8)
<b>pN<sup>2</sup></b>	
0	17 (32.1)
1	9 (17.0)
2	13 (24.5)
3	12 (22.6)
Nx	2 (3.8)
<b>Stage</b>	
I/II	27 (26.2)
III/IV	76 (73.8)
<b>HPV status<sup>3</sup></b>	
Positive	14/32 (43.7)
Negative	18/32 (56.3)

## Cancer localization

Oropharynx	32 (31.1)
Larynx	18 (17.5)
Oral cavity	31 (30.1)
Hypopharynx	15 (14.6)
Others <sup>4</sup>	7 (6.8)

## Type of treatment

Radiotherapy alone	6 (5.8)
Radiochemotherapy	44 (42.7)
Postoperative radiotherapy	15 (14.6)
Postoperative radiochemotherapy	38 (36.9)

## Surgery

Type of resection	
R0	25 (47.2)
R1	25 (47.2)
R2	3 (5.6)

## Systemic therapy

Chemotherapy	72 (69.9)
Cisplatin 100 mg/m <sup>2</sup>	66 (91.7)
Number of CDDP	
1	6 (9.2)
2	29 (44.6)
3	30 (46.1)
Cisplatin 40 mg/m <sup>2</sup>	3 (4.2)
Carboplatin AUC 2	1 (1.4)
Carboplatin AUC 5	2 (2.8)
Cetuximab	10 (9.7)

## Radiotherapy

Overall duration of radiotherapy, means±SD, days	48±7
<b>Total dose</b>	
70 Gy	57 (55.3)
66 Gy	46 (44.7)

## Fractionation schedule

2.12 Gy by fraction	56 (54.4)
2 Gy by fraction	47 (45.6)

## Total suspension of radiotherapy

Number of days of suspension, median [IQR]	3 [3-5]
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## Technique of radiotherapy

Tomotherapy	84 (81.6)
VMAT	19 (18.4)

## OAR doses

V20 oral cavity, means±SD, %	83.2±22.5
V30 oral cavity, means±SD, %	68.0±30.7

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**Table 1.** Baseline characteristics of patients, pathological features and treatments

	N(%) unless otherwise indicated		
Age, means±SD, years	63.0±8.9	<b>Cancer localization</b>	
BMI, means±SD, kg/m <sup>2</sup>	24.5±5.3	Oropharynx	32 (31.1)
Malnutrition <sup>1</sup>	15 (14.6)	Larynx	18 (17.5)
<b>Sex</b>		Oral cavity	31 (30.1)
Women	27 (26.2)	Hypopharynx	15 (14.6)
Men	76 (73.8)	Others <sup>4</sup>	7 (6.8)
<b>Performance status</b>		<b>Type of treatment</b>	
0	33 (32.0)	Radiotherapy alone	6 (5.8)
1	60 (58.3)	Radiochemotherapy	44 (42.7)
2	9 (8.7)	Postoperative radiotherapy	15 (14.6)
		Postoperative radiochemotherapy	38 (36.9)
<b>Smoking status</b>		<b>Surgery</b>	53 (51.5)
Never smokers	14 (13.6)	Type of resection	
Former smokers	60 (58.2)	R0	25 (47.2)
Active smokers	29 (28.2)	R1	25 (47.2)
Number of pack-years, median [IQR]	40 [35-50]	R2	3 (5.6)
Number of cigarettes/day, median [IQR]	6 [3-10]	<b>Systemic therapy</b>	
Former drinkers	29 (28.2)	Chemotherapy	72 (69.9)
Current drinkers	36 (34.9)	Cisplatin 100 mg/m <sup>2</sup>	66 (91.7)
<b>Diabetes</b>	14 (13.6)	Number of CDDP	
Metformin taking	12 (11.7)	1	6 (9.2)
<b>cT</b>		2	29 (44.6)
T1	10 (9.7)	3	30 (46.1)
T2	23 (22.3)	Cisplatin 40 mg/m <sup>2</sup>	3 (4.2)
T3	28 (27.2)	Carboplatin AUC 2	1 (1.4)
T4	37 (35.9)	Carboplatin AUC 5	2 (2.8)
Tx	5 (4.9)	Cetuximab	10 (9.7)
<b>cN</b>		<b>Radiotherapy</b>	
N0	40 (38.8)	Overall duration of radiotherapy, means±SD, days	48±7
N1	8 (7.8)	<b>Total dose</b>	
N2	46 (44.7)	70 Gy	57 (55.3)
N3	8 (7.8)	66 Gy	46 (44.7)
Nx	1 (1.0)	<b>Fractionation schedule</b>	
<b>pT<sup>2</sup></b>		2.12 Gy by fraction	56 (54.4)
T1	3 (5.7)	2 Gy by fraction	47 (45.6)
T2	15 (28.3)	<b>Total suspension of radiotherapy</b>	24 (23.3)
T3	19 (35.8)	Number of days of suspension, median [IQR]	3 [3-5]
T4	14 (26.4)	<b>Technique of radiotherapy</b>	
Tx	2 (3.8)	Tomotherapy	84 (81.6)
<b>pN<sup>2</sup></b>		VMAT	19 (18.4)
0	17 (32.1)	<b>OAR doses</b>	
1	9 (17.0)	V20 oral cavity, means±SD, %	83.2±22.5
2	13 (24.5)	V30 oral cavity, means±SD, %	68.0±30.7
3	12 (22.6)		
Nx	2 (3.8)		
<b>Stage</b>			
I/II	27 (26.2)		
III/IV	76 (73.8)		
<b>HPV status<sup>3</sup></b>			
Positive	14/32 (43.7)		
Negative	18/32 (56.3)		

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**Table 2.** Baseline characteristics of patients, pathological features and treatments according to smoking status

	Active Smokers N=29	Non-active Smokers N=74	P-value
<b>Age, means±SD, years</b>	59.3±8.8	64.4±8.6	<b>0.009</b>
<b>BMI, means±SD, kg/m<sup>2</sup></b>	22.5±5.1	25.3±5.1	<b>0.01</b>
<b>Malnutrition<sup>1</sup></b>	7 (24.1)	8 (10.8)	0.12
<b>Sex</b>			0.84
Women	8 (27.6)	19 (25.7)	
Men	21 (72.4)	55 (74.3)	
<b>Performance status</b>			0.05
0	7 (24.1)	26 (35.1)	
1	22 (75.9)	38 (51.3)	
2	0 (0.0)	9 (12.2)	
3	0 (0.0)	1 (1.4)	
4	0 (0.0)	0 (0.0)	
<b>Alcohol status</b>			<b>0.002</b>
Never drinkers/former drinkers	12 (41.4)	55 (74.3)	
Current drinkers	17 (58.6)	19 (25.7)	
<b>Diabetes</b>	1 (3.4)	13 (17.6)	0.11
Metformin taking	1 (100.0)	11 (84.6)	1.00
<b>cT</b>			0.18
T1	1 (3.4)	9 (12.2)	
T2	7 (24.1)	16 (21.6)	
T3	12 (41.4)	16 (21.6)	
T4	9 (31.0)	28 (37.8)	
Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
N1	2 (6.9)	6 (8.1)	
N2	14 (48.3)	32 (43.2)	
N3	3 (10.3)	5 (6.8)	
Nx	0 (0.0)	1 (1.3)	
<b>pT<sup>2</sup></b>			0.89
T1	0/7 (0.0)	3/46 (6.5)	
T2	2/7 (28.6)	13/46 (28.3)	
T3	2/7 (28.6)	17/46 (37.0)	
T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
Nx	1/7 (14.3)	1/46 (2.2)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
Negative	7/8 (87.5)	11/24 (45.8)	

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**Table 2.** Baseline characteristics of patients, pathological features and treatments according to smoking status

	Active Smokers N=29	Non-active Smokers N=74	P-value
<b>Age, means±SD, years</b>	<b>59.3±8.8</b>	<b>64.4±8.6</b>	<b>0.009</b>
<b>BMI, means±SD, kg/m<sup>2</sup></b>	22.5±3.1	25.3±5.1	<b>0.01</b>
<b>Malnutrition<sup>1</sup></b>	7 (24.1)	8 (10.8)	0.12
<b>Sex</b>			0.84
Women	8 (27.6)	19 (25.7)	
Men	21 (72.4)	55 (74.3)	
<b>Performance status</b>			0.05
0	7 (24.1)	26 (35.1)	
1	22 (75.9)	38 (51.3)	
2	0 (0.0)	9 (12.2)	
3	0 (0.0)	1 (1.4)	
4	0 (0.0)	0 (0.0)	
<b>Alcohol status</b>			<b>0.002</b>
Never drinkers/former drinkers	12 (41.4)	55 (74.3)	
Current drinkers	17 (58.6)	19 (25.7)	
<b>Diabetes</b>	1 (3.4)	13 (17.6)	0.11
Metformin taking	1 (100.0)	11 (84.6)	1.00
<b>cT</b>			0.18
T1	1 (3.4)	9 (12.2)	
T2	7 (24.1)	16 (21.6)	
T3	12 (41.4)	16 (21.6)	
T4	9 (31.0)	28 (37.8)	
Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
N1	2 (6.9)	6 (8.1)	
N2	14 (48.3)	32 (43.2)	
N3	3 (10.3)	5 (6.8)	
Nx	0 (0.0)	1 (1.3)	
<b>pT<sup>2</sup></b>			0.89
T1	0/7 (0.0)	3/46 (6.5)	
T2	2/7 (28.6)	13/46 (28.3)	
T3	2/7 (28.6)	17/46 (37.0)	
T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
Nx	1/7 (14.3)	1/46 (2.2)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
Negative	7/8 (87.5)	11/24 (45.8)	

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**Table 2.** Baseline characteristics of patients, pathological features and treatments according to smoking status

	Active Smokers N=29	Non-active Smokers N=74	P-value
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<b>BMI, mean±SD, kg/m<sup>2</sup></b>	<b>22.5±5.1</b>	<b>25.3±5.1</b>	<b>0.01</b>
<b>Malnutrition<sup>1</sup></b>	7 (24.1)	8 (10.8)	0.12
<b>Sex</b>			0.84
Women	8 (27.6)	19 (25.7)	
Men	21 (72.4)	55 (74.3)	
<b>Performance status</b>			0.05
0	7 (24.1)	26 (35.1)	
1	22 (75.9)	38 (51.3)	
2	0 (0.0)	9 (12.2)	
3	0 (0.0)	1 (1.4)	
4	0 (0.0)	0 (0.0)	
<b>Alcohol status</b>			<b>0.002</b>
Never drinkers/former drinkers	12 (41.4)	55 (74.3)	
Current drinkers	17 (58.6)	19 (25.7)	
<b>Diabetes</b>	1 (3.4)	13 (17.6)	0.11
Metformin taking	1 (100.0)	11 (84.6)	1.00
<b>cT</b>			0.18
T1	1 (3.4)	9 (12.2)	
T2	7 (24.1)	16 (21.6)	
T3	12 (41.4)	16 (21.6)	
T4	9 (31.0)	28 (37.8)	
Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
N1	2 (6.9)	6 (8.1)	
N2	14 (48.3)	32 (43.2)	
N3	3 (10.3)	5 (6.8)	
Nx	0 (0.0)	1 (1.3)	
<b>pT<sup>2</sup></b>			0.89
T1	0/7 (0.0)	3/46 (6.5)	
T2	2/7 (28.6)	13/46 (28.3)	
T3	2/7 (28.6)	17/46 (37.0)	
T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
Nx	1/7 (14.3)	1/46 (2.2)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
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**Table 2.** Baseline characteristics of patients, pathological features and treatments according to smoking status

	Active Smokers N=29	Non-active Smokers N=74	P-value
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<b>Sex</b>			0.84
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Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
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Nx	0 (0.0)	1 (1.3)	
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T1	0/7 (0.0)	3/46 (6.5)	
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T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
Nx	1/7 (14.3)	1/46 (2.2)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
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<b>Sex</b>			0.84
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T1	1 (3.4)	9 (12.2)	
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T3	12 (41.4)	16 (21.6)	
T4	9 (31.0)	28 (37.8)	
Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
N1	2 (6.9)	6 (8.1)	
N2	14 (48.3)	32 (43.2)	
N3	3 (10.3)	5 (6.8)	
Nx	0 (0.0)	1 (1.3)	
<b>pT<sup>2</sup></b>			0.89
T1	0/7 (0.0)	3/46 (6.5)	
T2	2/7 (28.6)	13/46 (28.3)	
T3	2/7 (28.6)	17/46 (37.0)	
T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
Nx	1/7 (14.3)	1/46 (2.2)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
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**Table 2.** Baseline characteristics of patients, pathological features and treatments according to smoking status

	Active Smokers N=29	Non-active Smokers N=74	P-value
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<b>Malnutrition<sup>1</sup></b>	7 (24.1)	8 (10.8)	0.12
<b>Sex</b>			0.84
Women	8 (27.6)	19 (25.7)	
Men	21 (72.4)	55 (74.3)	
<b>Performance status</b>			0.05
0	7 (24.1)	26 (35.1)	
1	22 (75.9)	38 (51.3)	
2	0 (0.0)	9 (12.2)	
3	0 (0.0)	1 (1.4)	
4	0 (0.0)	0 (0.0)	
<b>Alcohol status</b>			<b>0.002</b>
Never drinkers/former drinkers	12 (41.4)	55 (74.3)	
Current drinkers	17 (58.6)	19 (25.7)	
<b>Diabetes</b>	1 (3.4)	13 (17.6)	0.11
Metformin taking	1 (100.0)	11 (84.6)	1.00
<b>cT</b>			0.18
T1	1 (3.4)	9 (12.2)	
T2	7 (24.1)	16 (21.6)	
T3	12 (41.4)	16 (21.6)	
T4	9 (31.0)	28 (37.8)	
Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
N1	2 (6.9)	6 (8.1)	
N2	14 (48.3)	32 (43.2)	
N3	3 (10.3)	5 (6.8)	
Nx	0 (0.0)	1 (1.3)	
<b>pT<sup>2</sup></b>			0.89
T1	0/7 (0.0)	3/46 (6.5)	
T2	2/7 (28.6)	13/46 (28.3)	
T3	2/7 (28.6)	17/46 (37.0)	
T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
Negative	7/8 (87.5)	11/24 (45.8)	

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**Table 2.** Baseline characteristics of patients, pathological features and treatments according to smoking status

	Active Smokers N=29	Non-active Smokers N=74	P-value
<b>Age, means±SD, years</b>	59.3±8.8	64.4±8.6	<b>0.009</b>
<b>BMI, means±SD, kg/m<sup>2</sup></b>	22.5±5.1	25.3±5.1	<b>0.01</b>
<b>Malnutrition<sup>1</sup></b>	7 (24.1)	8 (10.8)	0.12
<b>Sex</b>			0.84
Women	8 (27.6)	19 (25.7)	
Men	21 (72.4)	55 (74.3)	
<b>Performance status</b>			0.05
0	7 (24.1)	26 (35.1)	
1	22 (75.9)	38 (51.3)	
2	0 (0.0)	9 (12.2)	
3	0 (0.0)	1 (1.4)	
4	0 (0.0)	0 (0.0)	
<b>Alcohol status</b>			<b>0.002</b>
Never drinkers/former drinkers	12 (41.4)	55 (74.3)	
Current drinkers	17 (58.6)	19 (25.7)	
<b>Diabetes</b>	1 (3.4)	13 (17.6)	0.11
Metformin taking	1 (100.0)	11 (84.6)	1.00
<b>cT</b>			0.18
T1	1 (3.4)	9 (12.2)	
T2	7 (24.1)	16 (21.6)	
T3	12 (41.4)	16 (21.6)	
T4	9 (31.0)	28 (37.8)	
Tx	0 (0.0)	5 (6.8)	
<b>cN</b>			0.90
N0	10 (34.5)	30 (40.5)	
N1	2 (6.9)	6 (8.1)	
N2	14 (48.3)	32 (43.2)	
N3	3 (10.3)	5 (6.8)	
Nx	0 (0.0)	1 (1.3)	
<b>pT<sup>2</sup></b>			0.89
T1	0/7 (0.0)	3/46 (6.5)	
T2	2/7 (28.6)	13/46 (28.3)	
T3	2/7 (28.6)	17/46 (37.0)	
T4	3/7 (42.8)	11/46 (23.9)	
Tx	0/7 (0.0)	2/46 (4.3)	
<b>pN<sup>2</sup></b>			0.31
0	1/7 (14.3)	16/46 (34.8)	
1	1/7 (14.3)	8/46 (17.4)	
2	3/7 (42.8)	10/46 (21.7)	
3	1/7 (14.3)	11/46 (23.9)	
<b>HVP status<sup>3</sup></b>			<b>0.04</b>
Positive	1/8 (12.5)	13/24 (54.2)	
Negative	7/8 (87.5)	11/24 (45.8)	

# Critère de jugement principal

**Table 3.** Events rates in smokers and non-smokers patients

	Events (%)		P-value	Adjusted-OR (95% CI)	P-value*
	Active Smokers N=29	Non-active Smokers N=74			
Severe acute toxicity	18 (62.1)	38 (51.3)	0.33	1.27 (0.47-3.40)	0.64
Severe mucositis	8 (27.6)	16 (21.6)	0.52	1.04 (0.34-3.22)	0.94
Severe dysphagia	10 (34.5)	28 (37.8)	0.75	0.60 (0.20-1.80)	0.36
Severe dermatitis	5 (17.2)	9 (12.2)	0.53	1.52 (0.40-5.73)	0.54

CI=confidence interval; OR=odds-ratio. \*Adjusted on age, BMI, current alcohol consumption and time since surgery

# Critères de jugement secondaires

**Table 3.** Events rates in smokers and non-smokers patients

	Events (%)		P-value	Adjusted-OR (95% CI)	P-value*
	Active Smokers N=29	Non-active Smokers N=74			
Severe acute toxicity	18 (62.1)	38 (51.3)	0.33	1.27 (0.47-3.40)	0.64
Severe mucositis	8 (27.6)	16 (21.6)	0.52	1.04 (0.34-3.22)	0.94
Severe dysphagia	10 (34.5)	28 (37.8)	0.75	0.60 (0.20-1.80)	0.36
Severe dermatitis	5 (17.2)	9 (12.2)	0.53	1.52 (0.40-5.73)	0.54

CI=confidence interval; OR=odds-ratio. \*Adjusted on age, BMI, current alcohol consumption and time since surgery

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

**Table 4.** Univariate and multivariate associations with occurrence of at least one severe acute toxicity

	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
			P-value	Adjusted OR (95% CI)	P-value
<b>Age, means±SD, years</b>	61.7±9.8	64.6±7.5	0.11	NS	NS
<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
Men	42 (75.0)	34 (72.3)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)			
<b>Smoking status</b>			0.33	-	-
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
<b>Stage</b>			0.45	-	-
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Surgery</b>	24 (42.9)	29 (61.7)	0.07	NS	NS
<b>Concurrent chemotherapy<sup>3</sup></b>	49 (87.5)	31 (66.0)	<b>0.009</b>	4.0 (1.4-11.7)	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
V20 oral cavity, means±SD, %	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

**Table 4.** Univariate and multivariate associations with occurrence of at least one severe acute toxicity

	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
			P-value	Adjusted OR (95% CI)	P-value
<b>Age, means±SD, years</b>	61.7±9.8	64.6±7.5	0.11	NS	NS
<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)		-	-
<b>Smoking status</b>			0.33		
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
<b>Stage</b>			0.45	-	-
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Surgery</b>	24 (42.9)	29 (61.7)	0.07	NS	NS
<b>Concurrent chemotherapy<sup>3</sup></b>	49 (87.5)	31 (66.0)	<b>0.009</b>	4.0 (1.4-11.7)	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
V20 oral cavity, means±SD, %	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

**Table 4.** Univariate and multivariate associations with occurrence of at least one severe acute toxicity

	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
			P-value	Adjusted OR (95% CI)	P-value
<b>Age, means±SD, years</b>	61.7±9.8	64.6±7.5	0.11	NS	NS
<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)		-	-
<b>Smoking status</b>			0.33		
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
<b>Stage</b>			0.45	-	-
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Surgery</b>	24 (42.9)	29 (61.7)	0.07	NS	NS
<b>Concurrent chemotherapy<sup>3</sup></b>	49 (87.5)	31 (66.0)	<b>0.009</b>	4.0 (1.4-11.7)	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
V20 oral cavity, means±SD, %	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

**Table 4.** Univariate and multivariate associations with occurrence of at least one severe acute toxicity

	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Multivariate analysis		
			Univariate analysis P-value	Adjusted OR (95% CI)	P-value
<b>Age, means±SD, years</b>	61.7±9.8	64.6±7.5	0.11	NS	NS
<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
Men	42 (75.0)	34 (72.3)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)		-	-
<b>Smoking status</b>			0.33	-	-
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Surgery</b>	24 (42.9)	29 (61.7)	0.07	NS	NS
<b>Concurrent chemotherapy<sup>3</sup></b>	49 (87.5)	31 (66.0)	<b>0.009</b>	4.0 (1.4-11.7)	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
V20 oral cavity, means±SD, %	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS



# Facteurs associés à la survenue de toxicité(s) aiguë(s)

**Table 4.** Univariate and multivariate associations with occurrence of at least one severe acute toxicity

	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
			P-value	Adjusted OR (95% CI)	P-value
<b>Age, means±SD, years</b>	61.7±9.8	64.6±7.5	0.11	NS	NS
<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
Men	42 (75.0)	34 (72.3)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)		-	-
<b>Smoking status</b>			0.33	-	-
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Surgery</b>	24 (42.9)	29 (61.7)	0.07	NS	NS
<b>Concurrent chemotherapy<sup>3</sup></b>	49 (87.5)	31 (66.0)	<b>0.009</b>	4.0 (1.4-11.7)	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
V20 oral cavity, means±SD, %	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

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	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
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<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
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<b>Performance status</b>			<b>0.09</b>	NS	NS
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2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)			
<b>Smoking status</b>			0.33	-	-
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
<b>Stage</b>			0.45	-	-
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Concurrent chemotherapy<sup>3</sup></b>	<b>49 (87.5)</b>	<b>31 (66.0)</b>	<b>0.009</b>	<b>4.0 (1.4-11.7)</b>	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
V20 oral cavity, means±SD, %	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

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	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
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<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
Men	42 (75.0)	34 (72.3)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)		-	-
<b>Smoking status</b>			0.33	-	-
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
<b>Metformin taking</b>	6 (10.7)	6 (12.8)	0.75	-	-
<b>cT</b>			<b>0.04</b>	NS	NS
T1	3 (5.4)	7 (14.9)			
T2	8 (14.3)	15 (31.9)			
T3	19 (33.9)	9 (19.1)			
T4	22 (39.3)	15 (31.9)			
Tx	4 (7.1)	1 (2.1)			
<b>Stage</b>			0.45	-	-
I/II	13 (23.2)	14 (29.8)			
III/IV	43 (76.8)	33 (70.2)			
<b>Cancer localization</b>			0.62	-	-
Oropharynx/larynx/oral cavity	43 (76.8)	38 (80.9)			
Others <sup>2</sup>	13 (23.2)	9 (19.1)			
<b>Surgery</b>	24 (42.9)	29 (61.7)	0.07	NS	NS
<b>Concurrent chemotherapy<sup>3</sup></b>	49 (87.5)	31 (66.0)	<b>0.009</b>	4.0 (1.4-11.7)	<b>0.01</b>
<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	36 (64.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>V20 oral cavity, means±SD, %</b>	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
<b>V30 oral cavity, means±SD, %</b>	73.9±28.6	61.1±31.9	0.06	NS	NS

# Facteurs associés à la survenue de toxicité(s) aiguë(s)

**Table 4.** Univariate and multivariate associations with occurrence of at least one severe acute toxicity

	At least one severe acute toxicity N=56	No severe acute toxicity N=47	Univariate analysis	Multivariate analysis	
			P-value	Adjusted OR (95% CI)	P-value
<b>Age, means±SD, years</b>	61.7±9.8	64.6±7.5	0.11	NS	NS
<b>BMI, means±SD, kg/m<sup>2</sup></b>	23.7±5.8	25.6±4.3	0.06	NS	NS
<b>Malnutrition<sup>1</sup></b>	11 (19.6)	4 (8.5)	0.11	NS	NS
<b>Sex</b>			0.76	-	-
Women	14 (25.0)	13 (27.7)			
Men	42 (75.0)	34 (72.3)			
<b>Performance status</b>			<b>0.09</b>	NS	NS
0	13 (23.2)	20 (42.6)			
1	37 (66.1)	23 (48.9)			
2	6 (10.7)	3 (6.4)			
3	0 (0.0)	1 (2.1)			
<b>Smoking status</b>			0.33	-	-
Non-active smokers	38 (67.9)	36 (76.6)			
Active smokers	18 (32.1)	11 (23.4)			
<b>Alcohol status</b>			0.51	-	-
Never drinkers/former drinkers	38 (67.9)	29 (61.7)			
Current drinkers	18 (32.1)	18 (38.3)			
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<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
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<b>V20 oral cavity, means±SD, %</b>	87.5±17.6	78.1±26.5	<b>0.04</b>	NS	NS
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<b>Sex</b>			0.76	-	-
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<b>Fractionation schedule</b>			<b>0.03</b>		<b>0.03</b>
2 Gy by fraction	20 (35.7)	27 (57.4)		1.00 (ref)	
2.12 Gy by fraction	26 (46.3)	20 (42.6)		2.4 (1.1-5.6)	
<b>OAR doses</b>					
<b>V20 oral cavity, means±SD, %</b>	<b>87.5±17.6</b>	<b>78.1±26.5</b>	<b>0.04</b>	NS	NS
V30 oral cavity, means±SD, %	73.9±28.6	61.1±31.9	0.06	NS	NS

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# Discussion

# Données de la littérature

- ❑ Association entre **tabagisme actif et mucites et dermites “sévères”** (p=0.03 et p<0.05)

*Porock D et al. (2004)<sup>1</sup>*

- ❑ Etude prospective (n = 53)
- ❑ Grade 2 considéré sévère
- ❑ Une seule évaluation à S5

- ❑ Association entre **tabagisme actif et durée de la mucite** (p=0.014)

*Rugg T et al. (1990)<sup>2</sup>*

- ❑ Etude rétrospective (n = 41)

<sup>1</sup>Porock D, Nikoletti S, Cameron F. The relationship between factors that impair wound healing and the severity of acute radiation skin and mucosal toxicities in head and neck cancer. *Cancer Nurs.* 2004 Feb;27(1):71–8.

<sup>2</sup>Rugg T, Saunders MI, Dische S. Smoking and mucosal reactions to radiotherapy. *Br J Radiol.* 1990 Jul;63(751):554–6.

# Données de la littérature

## Méta-analyse ne retrouvant **pas d'association** entre le **tabagisme actif** et la survenue de **toxicité(s) aiguë(s)**

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Smith J et al. (2019)<sup>1</sup>

**Table 3**

Acute and late toxicities for ceased and continuing smokers.

First Author (Year)	Outcome Measured	Acute Toxicity Rate Ceased Smokers (%)	Acute Toxicity Rate Continuing Smokers (%)	p value
<i>Acute Toxicities</i>				
Rugg (1990) [33]	Mucositis <sup>*</sup>	13.6wks	23.4wks	0.014
Zevallos (2009) [35]	Skin ≥ Grade II	43.2	31.8	0.29
	Mucositis ≥ Grade II	56.8	72.7	0.13
Chen (2011) [7]	≥Grade III	60	55	0.74
Meyer (2012) [36]	≥Grade III	22.3	24.1	0.65
Szeszko (2015) [37]	Mucositis ≥ Grade III	42	46	0.71
<i>Late Toxicities</i>				
Van der Voet (1998) [34]	10 yr Laryngeal Complications	14	28	NR
Chen (2011) [7]	≥Grade III	31	49	0.01
Meyer (2012) [36]	≥Grade III	3.5	4.5	0.61
<i>Specific Late Toxicities – ORN/CRN</i>				
Katsura (2008) [27]	ORN	3.8	38.5	0.011
Zevallos (2009) [35]	ORN	2.7	20.5	0.02
Chen (2011) [7]	ORN	4	5	NR
Raguse (2016) [38]	ORN	22.9	30.2	0.051
Sathasivam (2017) [40]	ORN	11	35.1	<0.001
Gessert (2017) [39]	CRN <sup>**</sup>	1.2	5.7	0.067

NR – Not recorded.

<sup>\*</sup> Reported as weeks to resolution of mucositis.

<sup>\*\*</sup> Chondroradionecrosis.

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Smith J et al. (2019)<sup>1</sup>

### ☐ Ostéoradionécrose

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# Données de la littérature

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Smith J et al. (2019)<sup>1</sup>

- Ostéoradionécrose
- Survie globale**

**Table 1**  
Overall survival (OS) data from included studies.

First Author (Year)	Follow-Up Period (Years)	OS Ceased Smokers (%)	OS Continuing Smokers (%)	p value
<i>Studies Included in Meta-Analysis</i>				
Browman (1993) [15]	2	66	39	0.005
Browman (2002) [16]	2	Light – 63.4	Heavy – 54.8	NR
Chen (2011) [7]	5	55	23	<0.001
Al-Mamgani (2013) [17]	10	68	33	<0.001
Platek (2016) [29]	5	70.7	32.1	NR
<i>Studies not in Meta-Analysis</i>				
Gillison (2012) [30]	9.3 <sup>*</sup>	HR – 2.19		<0.01
Choi (2016) [41]	4.5 <sup>*</sup>	HR <sup>**</sup> – 2.71 (Continuing), 2.38 (Ceased), 1.68 (Former)		All < 0.05
Descamps (2016) [32]	2 <sup>*</sup>	HR – 1.51		0.03

NR – Not recorded.

<sup>\*</sup> Reported as median follow-up.

<sup>\*\*</sup> Hazard ratios were reported in comparison to never smokers.

**Table 2**  
Locoregional control (LRC) data from included studies.

First Author (Year)	Follow-Up Period (Years)	LRC Ceased Smokers (%)	LRC Continuing Smokers (%)	p value
<i>Studies Included in Meta-Analysis</i>				
Terhaard (1991) [18]	3	96	85	<0.05
Benninger (1994) [19]	6.2 <sup>*</sup>	89.1	58.8	0.012
Colasanto (2004) [20]	16.6 <sup>*</sup>	91	90	0.30
Sjogren (2009) [22]	5	89	81	0.12
Chen (2011) [7]	5	69	58	0.03
Al-Mamgani (2013) [17]	10	89	66	<0.001
<i>Studies not in Meta-Analysis</i>				
Garden (2013) [31]	5	78	67	0.08
Zackrisson (2015) [28]	5 <sup>**</sup>	71.2	57.1	<0.001

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# Données de la littérature

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- Survie globale
- Contrôle locorégional**

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<sup>\*</sup> Reported as mean [19] and median [20] follow-up.

# Limites de l'étude

- ❑ Etude **monocentrique**
- ❑ Evaluation **subjective** de la consommation tabagique  
*Hald J et al. (2003)<sup>1</sup>*

<sup>1</sup>Hald J, Overgaard J, Grau C. Evaluation of objective measures of smoking status--a prospective clinical study in a group of head and neck cancer patients treated with radiotherapy. *Acta Oncol.* 2003;42(2):154-9.

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## Points forts de l'étude

- ❑ Etude **prospective**
- ❑ Résultats **concordants** avec la littérature
- ❑ **Evaluation de nos pratiques**

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# Conclusion



# Conclusion

- ❑ **Pas d'association significative mise en évidence** entre le tabagisme et la survenue d'une toxicité aiguë sévère en cours de Radiothérapie ORL
- ❑ **Chimiothérapie** et **dose par fraction** associées aux toxicités aiguës sévères
- ❑ **Suite** de l'étude : toxicités tardives, contrôle locorégional, survie sans progression et survie globale
- ❑ **Poursuite de la lutte anti-tabac**

# Merci pour votre attention

